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=> fil reg
FILE 'REGISTRY' ENTERED AT 15:38:22 ON 27 FEB 2006
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STRUCTURE FILE UPDATES:   26 FEB 2006  HIGHEST RN 875270-69-2
DICTIONARY FILE UPDATES:  26 FEB 2006  HIGHEST RN 875270-69-2

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d sta que 190
L88             STR
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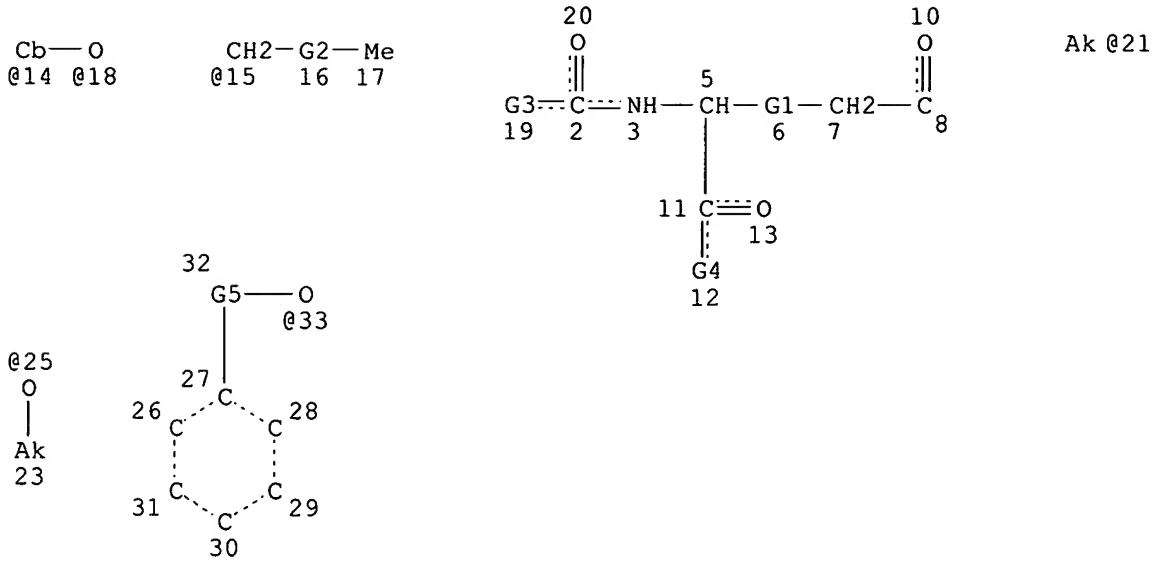

REP G1=(0-8) CH2
REP G2=(13-13) CH2
VAR G3=21/14/18/15
VAR G4=OH/25/33
REP G5=(0-1) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS PCY AT 14
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M17 C AT 14
ECOUNT IS M3 C AT 21

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L90 65123 SEA FILE=REGISTRY SSS FUL L88

100.0% PROCESSED 967046 ITERATIONS 65123 ANSWERS
SEARCH TIME: 00.00.45

=> d his

(FILE 'HOME' ENTERED AT 13:55:22 ON 27 FEB 2006)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:56:02 ON 27 FEB 2006
L1 1 S US20040115759/PN OR (US2003-671260# OR US2002-413684# OR DK20
E DUNWEBER D /AU
E DUENWEBER D /AU
L2 2 S E4
E DORTE/AU
E LUNOE/AU
E JENSEN I/AU

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L3          19 S E3,E6,E19,E20
               E JENSSEN I/AU
               E HOLM I/AU
L4          24 S E3,E8
               E HANSEN L/AU
L5         160 S E3,E6
               E HANSEN LOU/AU
L6          15 S E5,E6
               E BRAMMER/AU
L7           4 S E35
L8           6 S E60
               E BRAMER/AU
L9         228 S L2-L8
L10          1 S L1 AND L9
L11        227 S L9 NOT L10
               SEL RN L10

     FILE 'REGISTRY' ENTERED AT 14:08:09 ON 27 FEB 2006
L12          9 S E1-E9
L13          3 S 872-50-4 OR 109-99-9 OR 67-68-5
L14          3 S 7664-93-9 OR 75-75-2 OR 76-05-1
L15          5 S 89750-14-1 OR 141732-76-5 OR 89750-15-2 OR 9007-92-5 OR 9004-
L16          1 S 130391-54-7
L17          1 S L12 AND SQL/FA NOT L13-L16
L18         19 S HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK/SQSP
L19         19 S L17,L18

     FILE 'HCAPLUS' ENTERED AT 14:15:59 ON 27 FEB 2006
L20            TRA L11 1- RN :      838 TERMS

     FILE 'REGISTRY' ENTERED AT 14:16:05 ON 27 FEB 2006
L21        838 SEA L20
L22        832 S L21 NOT L12
L23        159 S L22 AND PROTEIN/FS
L24         14 S L23 AND (GLP OR GLUCAGON LIKE PEPTIDE)
               SEL RN 1-4
L25          4 S E20-E23
L26        804 S H.EGTFTSDVSSYLE.QAAKEFIAWLV.GR/SQSP
L27        140 S L26 AND (GLP OR GLUCAGON LIKE PEPTIDE)
L28         33 S L27 AND 7 AND 36
L29         44 S L27 AND 7 AND 37
L30         52 S L28,L29 AND SQL<=31
L31         23 S L28,L29 NOT L30
L32         17 S INSULIN(S)B30
L33       1008 S INSULIN(S)30B
L34       1017 S L32,L33
L35         31 S L34 AND DES
L36        391 S L34 AND DE
L37        391 S L35,L36
L38         25 S L37 NOT OX
L39        778 S L34 AND HUMAN
L40        235 S L39 AND L37
L41         11 S L40 AND DES B30
L42          0 S L40 AND DE B30 NOT L41

     FILE 'HCAPLUS' ENTERED AT 15:00:43 ON 27 FEB 2006
               E PEPTIDE/CT
L43        947 S PEPTIDE?/CT,CW (L) ACYL?
L44        306 S (L15 OR L16 OR L25 OR L30 OR L19) (L) ACYL?
L45       1237 S L43,L44
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                E SOLVENT/CT
L46           846 S E59-E61
L47          1116 S E75,E76
L48        112609 S SOLVENT#/CT,CW
L49          6621 S L48(L)(POLAR? OR APROT?)
L50             2 S L45 AND L46,L47,L49
L51             9 S L45 AND L13
L52            24 S L45 AND L14
L53             1 S L52 AND L50,L51

     FILE 'REGISTRY' ENTERED AT 15:07:07 ON 27 FEB 2006
L54             3 S 677326-61-3 OR 677326-57-7 OR 677326-60-2

     FILE 'HCAPLUS' ENTERED AT 15:07:26 ON 27 FEB 2006
L55             1 S L54
L56             1 S L53,L55

     FILE 'REGISTRY' ENTERED AT 15:07:52 ON 27 FEB 2006
L57             1 S 377780-60-4
L58             1 S 294855-91-7

     FILE 'HCAPLUS' ENTERED AT 15:10:25 ON 27 FEB 2006
L59             1 S L10,L53
L60             1 S L59 AND L1-L11,L43-L53,L55,L56,L59
L61             9 S L50,L51 NOT L60
                  SEL AN 2 3 5
L62             3 S L61 AND E1-E6
L63             4 S L60,L62

     FILE 'REGISTRY' ENTERED AT 15:14:35 ON 27 FEB 2006
L64             1 S 39416-73-4

     FILE 'HCAPLUS' ENTERED AT 15:15:06 ON 27 FEB 2006
L65            99 S L64
L66             3 S L65 AND L45,L47,L49
L67             6 S L63,L66
                  E ACYLATION/CT
                  E E3+ALL
L68         43018 S E2+NT
L69         12511 S E43+OLD,NT
L70         14365 S E44+OLD,NT
L71          2410 S E45+OLD,NT
L72           176 S L68-L71 AND (L15 OR L16 OR L25 OR L30 OR L19)
L73             1 S L72 AND L46,L47,L49
L74             3 S L65 AND L68-L71
L75             6 S L63,L73,L74
L76             4 S L75 AND L13,L14
L77             2 S L74 NOT L76
L78             1 S L77 AND 1995:721131/AN
L79             5 S L76,L78
L80             2 S LITHOCHOLOYL
                  SEL RN

     FILE 'REGISTRY' ENTERED AT 15:20:14 ON 27 FEB 2006
L81            91 S E1-E91
L82             1 S 57365-35-2
L83         84128 S 4432.3.1/RID
L84                STR
L85            50 S L84
L86                STR L84
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L87           50 S L86
L88              STR L86
L89           50 S L88
L90        65123 S L88 FUL
                 SAV TEMP L90 ABDEL671/A
L91            0 S L90 AND L19
L92           11 S L90 AND L21
L93            0 S L90 AND L34
L94           58 S L90 AND L83
L95           63 S L92,L94 NOT SQL/FA
L96         9409 S L90 NOT SQL/FA

     FILE 'HCAPLUS' ENTERED AT 15:31:21 ON 27 FEB 2006
L97           57 S L92,L95
L98         6815 S L96
L99            2 S L97 AND L68-L71
L100          65 S L98 AND L68-L71
L101           1 S L97 AND L13,L14
L102          88 S L98 AND L13,L14
L103          11 S L102,L100 AND L45
L104          14 S L79,L103
L105          14 S L104 AND L1-L11,L43-L53,L55,L56,L59-L63,L65-L80,L97-L104
L106          10 S L105 AND L13-L19,L25-L41,L54,L57,L58,L64
L107           4 S L105 NOT L106
L108           8 S L106 NOT COSMETIC?/TI

     FILE 'REGISTRY' ENTERED AT 15:38:22 ON 27 FEB 2006

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:38:29 ON 27 FEB 2006
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FILE COVERS 1907 - 27 Feb 2006  VOL 144 ISS 10
FILE LAST UPDATED: 26 Feb 2006  (20060226/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d l108 all hitstr tot

L108 ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2006 ACS on STN
AN   2005:451546  HCAPLUS
DN   143:3756
ED   Entered STN:  27 May 2005
TI   Making acylated insulin with use of selected protective peptide sequences
```

on glycine A1 and phenylalanine B1 in the two chain insulin intermediate

IN Kjeldsen, Thomas Borglum; Markussen, Jan

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N0015-17
ICS C07K0014-62; C12P0021-06

CC 9-16 (Biochemical Methods)
Section cross-reference(s): 2

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005047508	A1	20050526	WO 2004-DK782	20041111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DK 2003-1692 A 20031114

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005047508	ICM	C12N0015-17
	ICS	C07K0014-62; C12P0021-06
	IPCI	C12N0015-17 [ICM,7]; C07K0014-62 [ICS,7]; C12P0021-06 [ICS,7]
	IPCR	C07K0014-435 [I,C]; C07K0014-62 [I,A]; C12P0021-06 [I,A]; C12P0021-06 [I,C]
	ECLA	C07K014/62; C12P021/06

AB The present invention is related to a process for obtaining high yields of insulin or an insulin analog being acylated in an ε-amino group, in particular the ε-amino group in LysB29. In one aspect the present invention is related to a method for making acylated insulin or an acylated insulin analog wherein a two-chain insulin intermediate with N-terminal protecting peptide sequences attached to the B1 N-terminal amino acid group and to the A1 N-terminal amino acid group is acylated in a free ε-amino group whereupon the protecting peptide sequences are cleaved of and the desired acylated insulin is isolated. The authors have found that use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in the two chain insulin intermediate enables a nearly quant. acylation of the epsilon amino group of lysine B29 without using a large excess of the reagent, typically an N-hydroxysuccinimide ester of a fatty acid such as tetradecanoic acid. Both selected peptide sequences have either aspartic acid or glutamic acid residues as their free N-terminals, and arginine residues as their C-terminals where they are connected to the insulin B and A chain, resp. The number of the amino acid residues in the protecting amino acid sequences range from about 2 to about 10. In step i) the single-chain insulin precursor is cleaved between B29 lysine and the glutamic or aspartic acid residue constituting the N-terminal amino acid residue in the peptide sequence connecting B29 with A1. The single-chain insulin precursor is hereby opened rendering a two-chain insulin intermediate in which both N-terminals (the X1-X2 Arg

and the X3-X4 - Arg, resp.) are acidic amino acids. Proteases which cleave specifically at the carbonyl carbon of lysine are well known, in particular the lysine specific protease of Achromobacter lyticus. The advantage of having glutamic acid or aspartic acid as the N-terminals of the A- and B-chains in the opened precursor in step (a) or (ii) is that peptide bond formation between LysB29 and any of the N-terminals in the opened mol. is completely abolished. In step (a) or (ii) the insulin intermediate is acylated preferentially in the epsilon amino group of LysB29. The optimal conditions for the reaction is in mixts. of organic solvent and water at an apparent pH of about 10 when measured by a glass electrode.

ST acylated insulin protective peptide sequence glycineA1 phenylalanineB1 two chain; insulin acylation epsilon amino LysB29 protective peptide sequence; amino terminal protective peptide sequence insulin acylation LysB29

IT Fatty acids, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(N-hydroxysuccinimide ester of, acylating agent; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT Yeast
(cells transformed with vector comprising sequence encoding single-chain insulin precursor; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT Fatty acids, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(esters, acylating agent; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT Amides, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(fatty, acylating agent; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT **Acylation**
Protein sequences
(making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

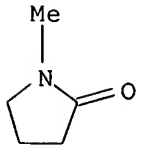
IT **Peptides, uses**
RL: NUU (Other use, unclassified); USES (Uses)
(making **acylated** insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT 9002-07-7, Trypsin
RL: CAT (Catalyst use); USES (Uses)
(-like protease, cleaving peptide btwn. Arg and B1 and between Arg and A1 in acylated intermediate; making acylated insulin with use of selected protective sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT 14464-31-4, Palmitic acid N-hydroxysuccinimide ester 14464-32-5, Stearic acid N-hydroxysuccinimide ester 14565-47-0 22102-66-5, Capric acid N-hydroxysuccinimide ester 69888-86-4, Tetradecanoic acid N-hydroxysuccinimide ester 201472-73-3, Heptadecanoic acid N-hydroxysuccinimide ester 823780-38-7, Pentadecanoic acid N-hydroxysuccinimide ester
RL: RGT (Reagent); RACT (Reactant or reagent)
(acylating agent; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)

IT 56-87-1, L-Lysine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of the epsilon amino group of; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
IT 852395-75-6 852395-77-8 852395-78-9 852395-79-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 68-12-2, uses 75-05-8, Acetonitrile, uses 75-65-0, uses
109-99-9, uses 123-91-1, 1,4-Dioxane, uses 127-19-5
872-50-4, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aqueous, acylation reaction carried out in; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
IT **9004-10-8**, Insulin, reactions
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(making **acylated** insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
IT 123175-82-6, Lysine specific protease
RL: CAT (Catalyst use); USES (Uses)
(of Achromobacter lyticus, cleaving the peptide bond in the acylated intermediate by; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hansen, L; WO 9802460 A 1998 HCAPLUS
(2) Kjeldsen, T; APPLIED MICROBIOLOGY AND BIOTECHNOLOGY 2000, V54, P277 HCAPLUS
(3) Kjeldsen, T; GENE 1996, V170(1), P107 HCAPLUS
(4) Kjeldsen, T; PROTEIN EXPRESSION AND PURIFICATION 1998, V14(3), P309 HCAPLUS
(5) Markussen, J; WO 9629344 A 1996 HCAPLUS
(6) Novo Industri AS; EP 0163529 A 1985 HCAPLUS
(7) Novo Nordisk AS; EP 1132404 A 2001 HCAPLUS
IT **109-99-9**, uses **872-50-4**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(aqueous, acylation reaction carried out in; making acylated insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
RN 109-99-9 HCAPLUS
CN Furan, tetrahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 872-50-4 HCAPLUS
CN 2-Pyrrolidinone, 1-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT **9004-10-8**, Insulin, reactions
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(making **acylated** insulin with use of selected protective peptide sequences on glycine A1 and phenylalanine B1 in two chain insulin intermediate)
RN 9004-10-8 HCAPLUS
CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:996208 HCAPLUS
DN 141:423388
ED Entered STN: 19 Nov 2004
TI Acylated lysobactin-type antibacterial nonadepsipeptides
IN Von, Nussbaum Franz; Brunner, Nina; Anlauf, Sonja; Endermann, Rainer; Fuerstner, Chantal; Hartmann, Elke; Koebberling, Johannes; Ragot, Jacques; Schiffer, Guido; Schuhmacher, Joachim; Svenstrup, Niels; Telser, Joachim; Bruening, Michael-Alexander
PA Bayer Healthcare AG, Germany
SO PCT Int. Appl., 260 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM C07K0011-02
ICS C07K0005-06; A61K0038-15
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 34, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004099239	A1	20041118	WO 2004-EP4416	20040427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10320781	A1	20041125	DE 2003-10320781	20030509
	CA 2524722	AA	20041118	CA 2004-2524722	20040427
	EP 1625153	A1	20060215	EP 2004-729639	20040427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 2005075281	A1	20050407	US 2004-840749	20040506
PRAI	DE 2003-10320781	A	20030509		
	WO 2004-EP4416	W	20040427		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004099239	ICM	C07K0011-02
	ICS	C07K0005-06; A61K0038-15
	IPCI	C07K0011-02 [ICM,7]; C07K0005-06 [ICS,7]; A61K0038-15 [ICS,7]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0005-00 [I,C]; C07K0005-06 [I,A]; C07K0005-065 [I,A]; C07K0011-00 [I,C]; C07K0011-02 [I,A]
	ECLA	C07K005/06A1A1; C07K005/06A1A2; C07K005/06A1B1; C07K005/06A1F1; C07K005/06A2; C07K011/02
DE 10320781	IPCI	C07K0011-02 [ICM,7]; A61K0031-395 [ICS,7]; A61P0031-00 [ICS,7]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0005-00 [I,C]; C07K0005-06 [I,A]; C07K0005-065 [I,A]; C07K0011-00 [I,C]; C07K0011-02 [I,A]
	ECLA	C07K005/06A1A1; C07K005/06A1A2; C07K005/06A1B1; C07K005/06A1F1; C07K005/06A2; C07K011/02
CA 2524722	IPCI	A61K0038-15 [I,A]; C07K0005-06 [I,A]; C07K0011-02 [I,A]
EP 1625153	IPCI	C07K0011-02 [ICM,7]; C07K0005-06 [ICS,7]; A61K0038-15 [ICS,7]
	ECLA	C07K005/06A1A1; C07K005/06A1A2; C07K005/06A1B1; C07K005/06A1F1; C07K005/06A2; C07K011/02
US 2005075281	IPCI	A61K0038-12 [ICM,7]; C07K0007-54 [ICS,7]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0005-00 [I,C]; C07K0005-06 [I,A]; C07K0005-065 [I,A]; C07K0011-00 [I,C]; C07K0011-02 [I,A]
	NCL	514/009.000
	ECLA	C07K005/06A1A1; C07K005/06A1A2; C07K005/06A1B1; C07K005/06A1F1; C07K005/06A2; C07K011/02

OS MARPAT 141:423388

AB The invention relates to lysobactin derived nonadepsipeptides, methods for the production thereof, and the use thereof for producing medicaments utilized in the treatment and/or prevention of diseases, especially infectious bacterial diseases.

ST lysobactin nonadepsipeptide acylation antibacterial

IT **Acylation**
Enterococcus faecalis
Enterococcus faecium
Fermentation
Ion exchange
Lysobacter
Nephrotoxicity
Peptide coupling
Size-exclusion chromatography
Staphylococcus aureus
Streptococcus pneumoniae
(**acylated** lysobactin-type antibacterial nonadepsipeptides)

IT Dipeptides
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT Polyoxyalkylenes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT **Peptides, biological studies**
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP

(Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(antimicrobial; **acylated** lysobactin-type antibacterial nonadepsipeptides)

IT **Peptides, biological studies**
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(cyclic; **acylated** lysobactin-type antibacterial nonadepsipeptides)

IT **Peptides, biological studies**
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(depsipeptides; **acylated** lysobactin-type antibacterial nonadepsipeptides)

IT Liquid chromatography
(flash; acylated lysobactin-type antibacterial nonadepsipeptides)

IT Preparative liquid chromatography
(high-performance reversed-phase; acylated lysobactin-type antibacterial nonadepsipeptides)

IT Drug delivery systems
(injections, i.v.; acylated lysobactin-type antibacterial nonadepsipeptides)

IT Drug delivery systems
(oral; acylated lysobactin-type antibacterial nonadepsipeptides)

IT Reversed phase HPLC
(preparative; acylated lysobactin-type antibacterial nonadepsipeptides)

IT Drug delivery systems
(tablets; acylated lysobactin-type antibacterial nonadepsipeptides)

IT 795312-09-3P
RL: BMF (Bioindustrial manufacture); BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 795312-10-6P
RL: BMF (Bioindustrial manufacture); CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 794595-27-0P 794595-31-6P 794595-57-6P 794595-67-8P 794595-69-0P
794595-81-6P 794595-97-4P 794596-15-9P 794596-17-1P 794596-35-3P
794596-41-1P 794596-45-5P 794596-57-9P 794596-59-1P 794596-69-3P
794596-85-3P 794596-93-3P 794597-13-0P 794597-17-4P 794597-19-6P
794597-27-6P 794597-31-2P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 1310-65-2, Lithium hydroxide
RL: CAT (Catalyst use); USES (Uses)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 67-56-1, Methanol, processes 67-64-1, Acetone, processes 9041-37-6, Sephadex LH 20 796070-87-6, Lewapol OC 1064 796070-88-7, Biotage Flash 75

RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 74086-61-6P 92463-61-1P 97642-16-5P 124215-72-1P 125447-43-0P
140834-91-9P 142148-66-1P 177913-93-8P, Benzyl 3-cyclopropyl-L-alaninate hydrochloride 794592-40-8P 794592-41-9P 794592-42-0P
794592-43-1P 794592-44-2P 794592-45-3P 794592-47-5P 794592-49-7P
794592-51-1P 794592-53-3P 794592-55-5P 794592-57-7P 794592-59-9P
794592-63-5P 794592-65-7P 794592-67-9P 794592-69-1P 794592-71-5P
794592-73-7P 794592-74-8P 794592-75-9P 794592-76-0P 794592-77-1P
794592-78-2P 794592-79-3P 794592-80-6P 794592-81-7P 794592-82-8P
794592-84-0P 794592-85-1P 794592-87-3P 794592-88-4P 794592-89-5P
794592-91-9P 794592-92-0P 794592-93-1P 794592-95-3P 794592-96-4P
794592-97-5P **794592-98-6P** 794592-99-7P 794593-01-4P
794593-02-5P 794593-03-6P 794593-04-7P 794593-05-8P 794593-06-9P
794593-07-0P 794593-08-1P 794593-09-2P 794593-10-5P 794593-11-6P
794593-12-7P 794593-13-8P 794593-15-0P 794593-16-1P 794593-17-2P
794593-18-3P 794593-19-4P 794593-20-7P 794593-21-8P 794593-22-9P
794593-23-0P 794593-24-1P 794593-25-2P 794593-26-3P 794593-27-4P
794593-28-5P **794593-29-6P** 794593-30-9P 794593-31-0P
794593-32-1P 794593-33-2P 794593-34-3P 794593-35-4P 794593-38-7P
794593-40-1P 794593-42-3P 794593-44-5P 794593-46-7P 794593-48-9P
794593-50-3P 794593-52-5P 794593-54-7P 794593-56-9P 794593-58-1P
794593-60-5P 794593-62-7P 794593-64-9P 794593-66-1P 794593-69-4P
794593-71-8P 794593-73-0P 794593-75-2P 794593-77-4P 794593-79-6P
794593-81-0P 794593-83-2P 794593-85-4P 794593-87-6P 794593-89-8P
794593-91-2P 794593-93-4P 794593-95-6P 794593-97-8P 794593-99-0P
794594-01-7P 794594-03-9P 794594-05-1P 794594-07-3P 794594-09-5P
794594-11-9P 794594-13-1P 794594-15-3P 794594-17-5P 794594-19-7P
794594-21-1P 794594-23-3P 794594-25-5P 794594-27-7P 794594-29-9P
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794594-93-7P 794594-95-9P 794594-97-1P 794594-99-3P 794595-01-0P
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795312-13-9P 795312-14-0P 795312-15-1P 795312-16-2P 795312-18-4P
795312-20-8P 795312-22-0P

RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 794595-29-2P 794595-33-8P 794595-35-0P 794595-37-2P 794595-39-4P
794595-41-8P 794595-43-0P 794595-45-2P 794595-47-4P 794595-49-6P
794595-51-0P 794595-53-2P 794595-55-4P 794595-59-8P 794595-61-2P
794595-63-4P 794595-65-6P 794595-71-4P 794595-73-6P 794595-75-8P
794595-77-0P 794595-79-2P 794595-83-8P 794595-85-0P 794595-87-2P
794595-89-4P 794595-91-8P 794595-93-0P 794595-95-2P 794595-99-6P
794596-01-3P 794596-03-5P 794596-05-7P 794596-07-9P 794596-09-1P
794596-11-5P 794596-13-7P 794596-19-3P 794596-21-7P 794596-23-9P
794596-25-1P 794596-27-3P 794596-29-5P 794596-31-9P 794596-33-1P
794596-37-5P 794596-39-7P 794596-43-3P 794596-47-7P 794596-49-9P
794596-51-3P 794596-53-5P 794596-55-7P 794596-61-5P 794596-63-7P
794596-65-9P 794596-67-1P 794596-71-7P 794596-73-9P 794596-75-1P
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794596-89-7P 794596-91-1P 794596-95-5P 794596-97-7P 794596-99-9P

794597-01-6P 794597-03-8P 794597-05-0P 794597-07-2P 794597-09-4P
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794597-29-8P 794597-33-4P 794597-35-6P 795312-24-2P 795312-26-4P
795312-28-6P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT **76-05-1**, Trifluoroacetic acid, reactions 80-70-6, N,N,N',N',-Tetramethylguanidine 122-03-2, 4-Isopropylbenzaldehyde 1738-69-8, L-Leucine benzyl ester 1947-42-8 2462-32-0, L-Phenylalanine benzyl ester, hydrochloride 3303-84-2 3350-20-7 4507-57-7 5241-64-5, N-(tert-Butoxycarbonyl)-D-tryptophan 5241-66-7, N-tert-Butoxycarbonyl-D-methionine 6140-64-3, 1-Methylcyclohexanecarboxaldehyde 6404-29-1, 6[(tert-Butoxycarbonyl)amino]hexanoic acid 13139-15-6, N-(tert-Butoxycarbonyl)-leucine 13139-16-7, N-(tert-Butoxycarbonyl)-L-isoleucine 13734-34-4, N-(tert-Butoxycarbonyl)-L-phenylalanine 13734-38-8, N-(tert-Butoxycarbonyl)-O-(tert-butyl)-L-serine 15761-39-4, N-(tert-Butoxycarbonyl)-L-proline 16937-92-1 16937-99-8, N-(tert-Butoxycarbonyl)-D-leucine 16947-84-5 17083-26-0 17193-40-7 18942-49-9, N-tert-Butoxycarbonyl-D-phenylalanine 22838-58-0, N-(tert-Butoxycarbonyl)-D-valine 24498-31-5 26250-84-0 27460-85-1 35661-40-6 37736-82-6 37784-17-1, N-(tert-Butoxycarbonyl)-D-proline 39895-10-8 40512-56-9 46460-82-6, O-Benzyl-L-serine-methyl ester 47173-80-8 48068-25-3 51186-58-4 55721-65-8, N-(tert-Butoxycarbonyl)-D-isoleucine 55780-90-0, N-(tert-Butoxycarbonyl)-D-alloisoleucine 55878-47-2 56558-30-6 57294-38-9, 4-[(tert-Butoxycarbonyl)amino]butanoic acid 63024-25-9 65806-90-8 66845-42-9 69355-99-3 70642-86-3, N-tert-Butoxycarbonyl-D-tyrosine 71066-00-7 71989-23-6, N-(9-Fluorenylmethoxycarbonyl)-L-isoleucine 71989-33-8 71989-38-3 76985-10-9, N-tert-Butoxycarbonyl-3-(2-naphthyl)-D-alanine 79777-82-5 82732-07-8 88568-95-0 88950-64-5, 1-[tert-Butoxycarbonyl)amino]cyclopropane carboxylic acid 89536-84-5 95753-55-2 96314-29-3 98266-33-2 112455-83-1 112695-98-4 114873-10-8 127095-92-5 128779-47-5 132684-59-4 138022-95-4 143824-78-6 147923-08-8 153152-15-9 172843-97-9 173204-44-9 177164-50-0 189619-55-4 200872-45-3 213343-66-9 230294-73-2 262301-38-2 288159-40-0 406681-37-6 753441-74-6 794592-61-3 794592-83-9 794592-86-2 794592-90-8 794593-36-5 794593-67-2 794594-36-8 794597-36-7
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)

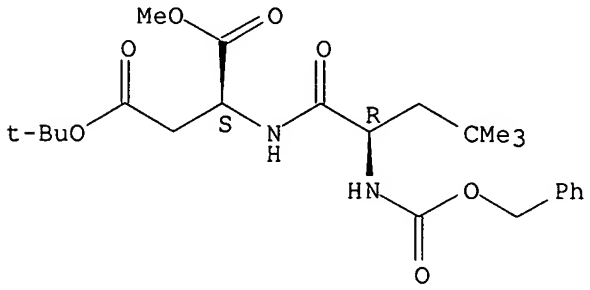
IT 794593-00-3P 794593-14-9P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)

IT 64-17-5, Ethanol, biological studies 557-04-0, Magnesium stearate 9003-39-8 9005-25-8, Starch, biological studies 11138-66-2, Xanthan gum 25322-68-3, Polyethyleneglycol 64044-51-5
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acylated lysobactin-type antibacterial nonadepsipeptides)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Egner, B; TETRAHEDRON 1997, V53(41), P14021 HCAPLUS
(2) Harada, K; JOURNAL OF CHROMATOGRAPHY A 2001, V932(1-2), P75 HCAPLUS
(3) Palomo, C; TETRAHEDRON LETTERS 2001, V42(51), P8955 HCAPLUS

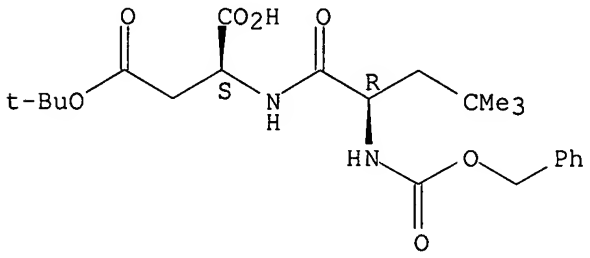
(4) Tymiak, A; JOURNAL OF ORGANIC CHEMISTRY 1989, V54(5), P1149 HCAPLUS
(5) Tymiak, A; JOURNAL OF ORGANIC CHEMISTRY 1989, V54(5), P1149 HCAPLUS
IT **794592-98-6P 794593-29-6P**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)
RN 794592-98-6 HCAPLUS
CN L-Aspartic acid, 4-methyl-N-[(phenylmethoxy)carbonyl]-D-leucyl-, 24-(1,1-dimethylethyl) 21-methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

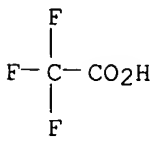


RN 794593-29-6 HCAPLUS
CN L-Aspartic acid, 4-methyl-N-[(phenylmethoxy)carbonyl]-D-leucyl-, 24-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **76-05-1**, Trifluoroacetic acid, reactions
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(acylated lysobactin-type antibacterial nonadepsipeptides)
RN 76-05-1 HCAPLUS
CN Acetic acid, trifluoro- (8CI, 9CI) (CA INDEX NAME)



L108 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:292034 HCAPLUS

DN 140:317698
ED Entered STN: 09 Apr 2004
TI Method for producing acylated peptides
IN **Duenweber, Dorte Lunoe; Jensen, Inge Holm; Hansen, Louis Brammer**
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K0001-00
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 2, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004029077	A2	20040408	WO 2003-DK629	20030925 <--
	WO 2004029077	A3	20040513		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2500123	AA	20040408	CA 2003-2500123	20030925 <--
	AU 2003266218	A1	20040419	AU 2003-266218	20030925 <--
	US 2004115759	A1	20040617	US 2003-671260	20030925 <--
	EP 1546090	A2	20050629	EP 2003-798091	20030925 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003014289	A	20050726	BR 2003-14289	20030925 <--
PRAI	DK 2002-1421	A	20020925 <--		
	US 2002-413684P	P	20020926 <--		
	WO 2003-DK629	W	20030925		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004029077	ICM	C07K0001-00
	IPCI	C07K0001-00 [ICM,7]
	IPCR	C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-575 [I,A]; C07K0014-605 [I,A]; C07K0014-62 [I,A]; G01N0033-68 [I,A]; G01N0033-68 [I,C]
	ECLA	C07K001/107D4; C07K014/575L; C07K014/605; C07K014/62; G01N033/68 <--
CA 2500123	IPCI	C07C0235-72 [ICM,7]; C07K0001-06 [ICS,7]; A61K0038-28 [ICS,7]; C07K0014-605 [ICS,7]; C07K0014-62 [ICS,7]; G01N0033-68 [ICS,7]
	IPCR	C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-575 [I,A]; C07K0014-605 [I,A]; C07K0014-62 [I,A]; G01N0033-68 [I,A]; G01N0033-68 [I,C] <--
AU 2003266218	IPCI	C07K0001-00 [ICM,7] <--
US 2004115759	IPCI	C12P0021-06 [ICM,7]
	IPCR	C07K0001-00 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-575 [I,A]; C07K0014-605 [I,A]; C07K0014-62 [I,A]; G01N0033-68

[I,A]; G01N0033-68 [I,C]
NCL 435/068.100
ECLA C07K001/00B; C07K001/107D4; C07K014/575L; C07K014/605; C07K014/62; G01N033/68 <--
EP 1546090 IPCI C07C0235-72 [ICM,7]; C07K0001-06 [ICS,7]; G01N0033-68 [ICS,7]; A61K0038-28 [ICS,7]; C07K0014-605 [ICS,7]; C07K0014-62 [ICS,7]
IPCR C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-575 [I,A]; C07K0014-605 [I,A]; C07K0014-62 [I,A]; G01N0033-68 [I,A]; G01N0033-68 [I,C]
ECLA C07K001/107D4; C07K014/575L; C07K014/605; C07K014/62; G01N033/68 <--
BR 2003014289 IPCI C07K0001-00 [ICM,7]
ECLA C07K001/107D4; C07K014/575L; C07K014/605; C07K014/62; G01N033/68 <--

OS MARPAT 140:317698

AB The present invention provides a method for acylating one or more amino groups of a peptide where the acylation reaction is to be performed in an aqueous mixture containing less than 10 %weight/weight aprotic polar solvent. Recombinant Arg34GLP-1(7-37) was dissolved in 0.1 mol/kg triethylamine (23 mL) at 10-15 °C. N-hexadecanoylglutamic acid γ-N-hydroxysuccinimide ester (63.7 mg, 0.13 mmol) was added. After 20 min at room temperature water (42 mL) was added, and the pH was adjusted to 8.0 by addition of 1.0 M acetic acid. The reaction mixture was shown to contain 84 % (by area) of Arg34Lys26-[N-ε-[γ-Glu(N-hexadecanoyl)]]-GLP-1(7-37) and 0.5 % (by area) of Arg34Lys26-[N-ε-(α-Glu(N-hexadecanoyl))]-GLP-1(7-37).

ST acylated peptide; GLP1 acylation hexadecanoylglutamate hydroxysyccinimide ester

IT **Acylation**
Human
(acylated peptides production in aqueous mixture containing acylating agent and low amount of aprotic polar solvent)

IT **Peptides, preparation**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**acylated**; **acylated** peptides production in aqueous mixture containing **acylating** agent and low amount of aprotic polar solvent)

IT Acids, uses
RL: NUU (Other use, unclassified); USES (Uses)
(acylating agent stabilization with; acylated peptides production in aqueous mixture containing acylating agent and low amount of aprotic polar solvent)

IT **Peptides, reactions**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**acylation** of; **acylated** peptides production in aqueous mixture containing **acylating** agent and low amount of aprotic polar solvent)

IT **Acylation**
(agents; acylated peptides production in aqueous mixture containing acylating agent and low amount of aprotic polar solvent)

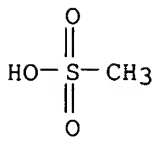
IT **Polar solvents**
(**aprotic**; acylated peptides production in aqueous mixture containing acylating agent and low amount of **aprotic polar** solvent)

IT Buffers
(in reaction mixture for maintaining pH; acylated peptides production in aqueous mixture containing acylating agent and low amount of aprotic polar solvent)

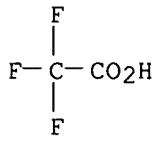
IT **677326-61-3P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(acylated peptides production in aqueous mixture containing acylating agent and low
amount of aprotic polar solvent)
IT **75-75-2**, Methanesulfonic acid **76-05-1**, Trifluoroacetic
acid, uses **7664-93-9**, Sulfuric acid, uses
RL: NUU (Other use, unclassified); USES (Uses)
(acylating agent stabilization with; acylated peptides production in aqueous
mixture containing acylating agent and low amount of aprotic polar solvent)
IT **677326-57-7**, (1A-21A),(1B-29B)-Insulin (human) **677326-59-9**
677326-59-9D, analogs **677326-60-2**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(**acylation** of; **acylated** peptides production in aqueous
mixture containing **acylating** agent and low amount of aprotic polar
solvent)
IT **9004-10-8**, Insulin, reactions **9004-10-8D**, Insulin,
analogs and derivs. **9007-92-5**, Glucagon, reactions
9007-92-5D, Glucagon, analogs and derivs. **89750-14-1**,
GLP-1 **89750-14-1D**, GLP-1, agonists, analogs and derivs.
89750-15-2, Glucagon-like peptide II **89750-15-2D**,
Glucagon-like peptide II, analogs and derivs. **130391-54-7**,
Exendin-3 **141732-76-5**, Exendin-4 **141732-76-5D**,
Exendin-4, analogs and derivs.
RL: RCT (Reactant); RACT (Reactant or reagent)
(**acylation** of; **acylated** peptides production in aqueous
mixture containing **acylating** agent and low amount of aprotic polar
solvent)
IT **377780-60-4**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(as acylating agent; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
IT **294855-91-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(as acylating agent; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
IT **67-68-5**, Dimethylsulfoxide, uses **109-99-9**,
Tetrahydrofuran, uses **872-50-4**, N-Methyl-2-pyrrolidone, uses
RL: NUU (Other use, unclassified); USES (Uses)
(as aprotic polar solvent; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
IT 121-44-8, Triethylamine, uses
RL: NUU (Other use, unclassified); USES (Uses)
(reaction solution containing; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
IT **677326-61-3P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(acylated peptides production in aqueous mixture containing acylating agent and low
amount of aprotic polar solvent)
RN 677326-61-3 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **75-75-2**, Methanesulfonic acid **76-05-1**, Trifluoroacetic
acid, uses **7664-93-9**, Sulfuric acid, uses

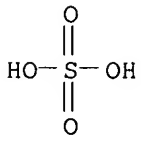
RL: NUU (Other use, unclassified); USES (Uses)
(acylating agent stabilization with; acylated peptides production in aqueous mixture containing acylating agent and low amount of aprotic polar solvent)
RN 75-75-2 HCAPLUS
CN Methanesulfonic acid (8CI, 9CI) (CA INDEX NAME)



RN 76-05-1 HCAPLUS
CN Acetic acid, trifluoro- (8CI, 9CI) (CA INDEX NAME)



RN 7664-93-9 HCAPLUS
CN Sulfuric acid (8CI, 9CI) (CA INDEX NAME)



IT **677326-57-7**, (1A-21A),(1B-29B)-Insulin (human) **677326-59-9** **677326-59-9D**, analogs **677326-60-2**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(**acylation** of; **acylated** peptides production in aqueous mixture containing **acylating** agent and low amount of aprotic polar solvent)
RN 677326-57-7 HCAPLUS
CN (1A-21A),(1B-29B)-Insulin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 677326-59-9 HCAPLUS
CN L-Lysinamide, L-histidylglycyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-leucyl-L-seryl-L-lysyl-L-glutaminyl-L-methionyl-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-alanyl-L-valyl-L-arginyl-L-leucyl-L-phenylalanyl-L-isoleucyl-L-α-glutamyl-L-tryptophyl-L-leucyl-L-lysyl-L-asparaginylglycylglycyl-L-prolyl-L-seryl-L-serylglycyl-L-alanyl-L-prolyl-L-prolyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 677326-59-9 HCAPLUS
CN L-Lysinamide, L-histidylglycyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-leucyl-L-seryl-L-

lysyl-L-glutaminyl-L-methionyl-L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-alanyl-L-valyl-L-arginyl-L-leucyl-L-phenylalanyl-L-isoleucyl-L-α-glutamyl-L-tryptophyl-L-leucyl-L-lysyl-L-asparaginylglycylglycyl-L-prolyl-L-seryl-L-serylglycyl-L-alanyl-L-prolyl-L-prolyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 677326-60-2 HCAPLUS
CN (1A-21A),(1B-29B)-Insulin (human), sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9004-10-8**, Insulin, reactions **9004-10-8D**, Insulin, analogs and derivs. **9007-92-5**, Glucagon, reactions **9007-92-5D**, Glucagon, analogs and derivs. **89750-14-1**, GLP-1 **89750-14-1D**, GLP-1, agonists, analogs and derivs. **89750-15-2**, Glucagon-like peptide II **89750-15-2D**, Glucagon-like peptide II, analogs and derivs. **130391-54-7**, Exendin-3 **141732-76-5**, Exendin-4 **141732-76-5D**, Exendin-4, analogs and derivs.
RL: RCT (Reactant); RACT (Reactant or reagent)
(**acylation** of; **acylated** peptides production in aqueous mixture containing **acylating** agent and low amount of aprotic polar solvent)
RN 9004-10-8 HCAPLUS
CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9004-10-8 HCAPLUS
CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9007-92-5 HCAPLUS
CN Glucagon (7CI, 8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9007-92-5 HCAPLUS
CN Glucagon (7CI, 8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 89750-15-2 HCAPLUS
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 89750-15-2 HCAPLUS
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 130391-54-7 HCAPLUS
CN Exendin 3 (9CI) (CA INDEX NAME)

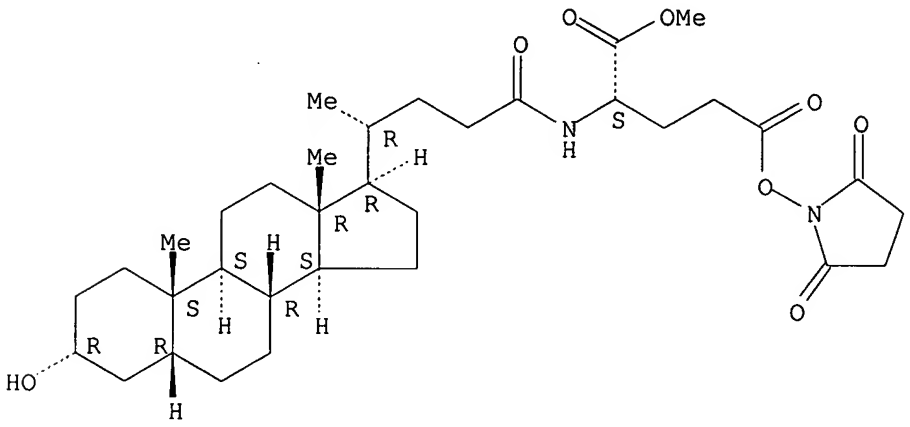
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 141732-76-5 HCAPLUS
CN Exendin 4 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 141732-76-5 HCAPLUS
CN Exendin 4 (9CI) (CA INDEX NAME)

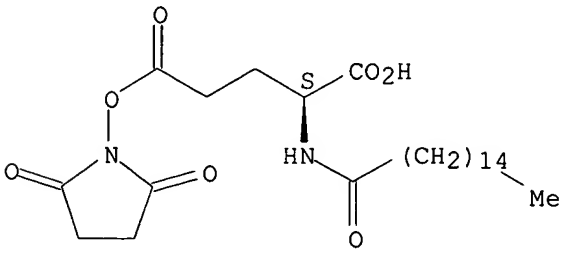
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **377780-60-4**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(as acylating agent; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
RN 377780-60-4 HCAPLUS
CN L-Norvaline, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-N-[(3α,5β)-3-hydroxy-24-oxocholan-24-yl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



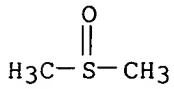
IT **294855-91-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(as acylating agent; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
RN 294855-91-7 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-2-[(1-oxohexadecyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



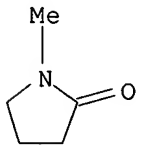
IT **67-68-5**, Dimethylsulfoxide, uses **109-99-9**, Tetrahydrofuran, uses **872-50-4**, N-Methyl-2-pyrrolidone, uses

RL: NUU (Other use, unclassified); USES (Uses)
(as aprotic polar solvent; acylated peptides production in aqueous mixture containing
acylating agent and low amount of aprotic polar solvent)
RN 67-68-5 HCAPLUS
CN Methane, sulfinylbis- (9CI) (CA INDEX NAME)



RN 109-99-9 HCAPLUS
CN Furan, tetrahydro- (7CI, 8CI, 9CI) (CA INDEX NAME)

RN 872-50-4 HCAPLUS
CN 2-Pyrrolidinone, 1-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L108 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2003:97435** HCAPLUS
DN 138:149946
ED Entered STN: 07 Feb 2003
TI Production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension
IN Diers, Ivan; Balschmidt, Per; Markussen, Jan; Jonassen, Ib; Egel-Mitani, Michi; Kjeldsen, Thomas Borglum
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K0001-00
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 3, 6, 34
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003010186	A2	20030206	WO 2002-DK502	20020718
WO 2003010186	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	CA 2452735	AA	20030206	CA 2002-2452735	20020718
	EP 1421103	A2	20040526	EP 2002-750842	20020718
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	BR 2002011346	A	20040921	BR 2002-11346	20020718
	CN 1558912	A	20041229	CN 2002-818726	20020718
	JP 2005504527	T2	20050217	JP 2003-515545	20020718
	US 2003144471	A1	20030731	US 2002-205110	20020724
PRAI	DK 2001-1141	A	20010724		
	US 2001-310793P	P	20010808		
	WO 2002-DK502	W	20020718		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003010186	ICM	C07K0001-00
	IPCI	C07K0001-00 [ICM,7]
	ECLA	C07K001/00B; C07K001/107D4; C07K014/605
CA 2452735	IPCI	C07K0001-00 [ICM,7]
EP 1421103	IPCI	C07K0001-00 [ICM,7]; C07K0014-605 [ICS,7]
	IPCR	C07K0001-00 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-605 [I,A]
BR 2002011346	IPCI	C07K0001-00 [ICM,7]; C07K0014-605 [ICS,7]
CN 1558912	IPCI	C07K0001-00 [ICM,7]; C07K0014-605 [ICS,7]
JP 2005504527	IPCI	C12P0021-02; C07K0014-47; C12N0015-09
	FTERM	4B024/AA20; 4B024/BA80; 4B024/CA02; 4B024/CA05; 4B024/DA06; 4B024/DA12; 4B024/HA01; 4B024/HA11; 4B064/AG01; 4B064/CA19; 4B064/CC24; 4B064/DA13; 4H045/AA10; 4H045/AA20; 4H045/AA30; 4H045/BA10; 4H045/CA40; 4H045/EA20; 4H045/EA50; 4H045/FA74
US 2003144471	IPCI	A01N0037-18 [ICM,7]; A61K0038-00 [ICS,7]; C07K0002-00 [ICS,7]
	IPCR	C07K0001-00 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]
	NCL	530/300.000
	ECLA	C07K001/00B; C07K001/107D4

OS MARPAT 138:149946

AB The present invention is related to a method of producing polypeptides in transformed host cells by expressing a precursor mol. of the desired polypeptide which is to be acylated at certain lysine ε-amino groups in a subsequent in vitro step. The N-terminal extensions allow for preferential acylation of the expressed precursor mol. and protects the expressed precursor mol. against proteolytic degradation within the host cell or in the culture medium. In addition, the precursor mol. is easier to purify and has a decreased tendency to form fibrils, thus allowing more flexibility when selecting down-stream separation and purification steps in large scale operations. The invention is also related to DNA sequences, vectors, and transformed host cells for use in the claimed method. Further, the present invention is related to certain precursors of the desired polypeptides and certain acylation methods. Thus EEAHK-Arg34(glucagon-like peptide I)(7-37)-Lys26 γ-Glu-hexadecanoyl is produced in 52% yield with acylation of the N-terminal extended GLP-1(7-37) with Glu(ONSu)N-hexadecanoyl Me ester in the presence of 2 equiv of Zn2+ in CH3CN.

ST protein acylation precursor cloning proteolytic cleavage; glucagon like peptide acylation precursor cloning cleavage

IT Protein motifs
(N-terminal extension; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT Metals, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(acylation at lysine ε-amino group in presence of; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT Albumins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(metal-binding site from; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT **Solvents**
(organic, acylation at lysine ε-amino group in presence of; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT **Acylation**
Molecular cloning
(production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT Proteins
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT Fermentation
(protein; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT Saccharomyces cerevisiae
Yeast
(recombinant expression host; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT 54017-28-6 111543-77-2 191600-12-1 209733-99-3 433919-30-3
477883-84-4 494863-26-2 494863-28-4 494863-30-8 494863-32-0
494863-35-3 494863-38-6 494863-40-0 494863-42-2 494863-43-3
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494863-50-2 494863-51-3 494863-52-4 494863-53-5 494863-54-6
494863-55-7 494863-56-8 494863-57-9 494863-59-1 494863-60-4
494863-63-7 494863-65-9 494863-66-0 494863-67-1 494863-69-3
494863-71-7 494863-72-8 494863-73-9 494863-74-0 494863-75-1
494863-76-2 494863-77-3 494863-79-5 494863-80-8 494863-81-9
494863-82-0 494863-83-1 494863-84-2 496826-87-0 496826-88-1
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(N-terminal extension; production of acylated polypeptides by recombinant

expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT 75-05-8, Acetonitrile, reactions **872-50-4**, N-Methylpyrrolidone, reactions 7439-89-6, Iron, reactions 7439-95-4, Magnesium, reactions 7439-96-5, Manganese, reactions 7440-02-0, Nickel, reactions 7440-48-4, Cobalt, reactions 7440-50-8, Copper, reactions 7440-66-6, Zinc, reactions 7440-70-2, Calcium, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(acylation at lysine ε-amino group in presence of; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT 56-87-1, L-Lysine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation at ε-amino group of; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT **204521-63-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT **496765-91-4P 496765-92-5P 496765-93-6P**
496765-94-7P 496765-95-8P 496765-96-9P
496765-97-0P 496765-98-1P 496765-99-2P
496766-00-8P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; production of **acylated** polypeptides by recombinant expression of precursor proteins followed by **acylation** at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT **106612-94-6P**, 7-37-Glucagon-like peptide I (human)
204521-68-6P 494823-59-5P 494823-60-8P
494823-61-9P 494823-62-0P 494823-63-1P
494823-64-2P 494823-65-3P 494823-66-4P
494823-67-5P 494823-68-6P 494823-69-7P
494823-70-0P 494823-71-1P 494823-72-2P
494823-73-3P 494823-74-4P 494823-75-5P
494823-76-6P 494823-77-7P 494823-78-8P
494823-79-9P 494823-80-2P 494823-81-3P
494823-82-4P 494823-83-5P 494823-84-6P
494823-85-7P 494823-86-8P 494823-87-9P
494823-88-0P 494823-89-1P 494823-90-4P
494823-91-5P 494823-92-6P 494823-93-7P
494823-94-8P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; production of **acylated** polypeptides by recombinant expression of precursor proteins followed by **acylation** at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT 9002-08-8, Trypsinogen
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(calcium-binding site from; production of acylated polypeptides by

recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

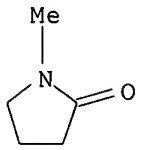
IT 9014-74-8, Enterokinase 123175-82-6, Lysine-specific proteinase
RL: CAT (Catalyst use); USES (Uses)
(cleavage by; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT 9034-39-3P, Growth hormone-releasing hormone **89750-14-1P**, Glucagon-like peptide I **89750-15-2P**, Glucagon-like peptide II
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(production of **acylated** polypeptides by recombinant expression of precursor proteins followed by **acylation** at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT 81669-70-7, Metalloproteinase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(zinc-binding site from; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

IT **872-50-4**, N-Methylpyrrolidone, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(acylation at lysine ε-amino group in presence of; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

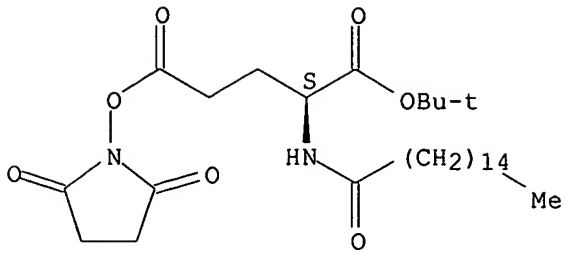
RN 872-50-4 HCAPLUS
CN 2-Pyrrolidinone, 1-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT **204521-63-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation by; production of acylated polypeptides by recombinant expression of precursor proteins followed by acylation at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

RN 204521-63-1 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-2-[(1-oxohexadecyl)amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **496765-91-4P 496765-92-5P 496765-93-6P**
496765-94-7P 496765-95-8P 496765-96-9P
496765-97-0P 496765-98-1P 496765-99-2P
496766-00-8P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; production of **acylated** polypeptides by recombinant expression of precursor proteins followed by **acylation** at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

RN 496765-91-4 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 496765-92-5 HCAPLUS
CN Glycine, L-α-aspartyl-L-α-aspartyl-L-α-aspartyl-L-α-aspartyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 496765-93-6 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-leucyl-L-α-aspartyl-L-alanyl-L-arginyl-L-leucyl-L-α-glutamyl-L-alanyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 496765-94-7 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-methionyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA

INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496765-95-8 HCAPLUS
CN Glycine, L-α-aspartyl-L-α-aspartyl-L-α-aspartyl-L-α-aspartyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496765-96-9 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-leucyl-L-α-aspartyl-L-alanyl-L-arginyl-L-leucyl-L-α-glutamyl-L-alanyl-L-leucyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496765-97-0 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-methionyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496765-98-1 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496765-99-2 HCAPLUS
CN Glycine, N-(1-oxohexadecyl)-L-γ-glutamyl-L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496766-00-8 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-

N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

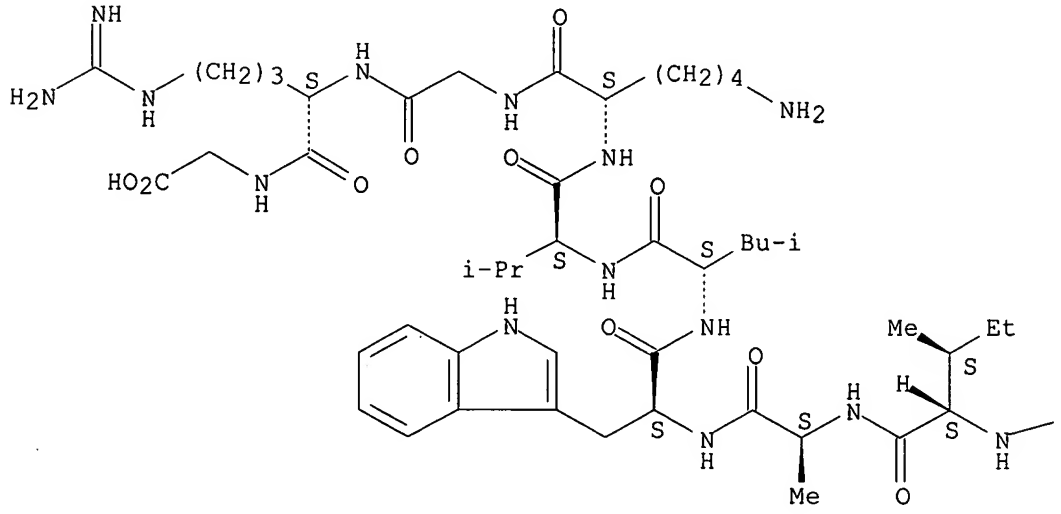
IT **106612-94-6P**, 7-37-Glucagon-like peptide I (human)
204521-68-6P 494823-59-5P 494823-60-8P
494823-61-9P 494823-62-0P 494823-63-1P
494823-64-2P 494823-65-3P 494823-66-4P
494823-67-5P 494823-68-6P 494823-69-7P
494823-70-0P 494823-71-1P 494823-72-2P
494823-73-3P 494823-74-4P 494823-75-5P
494823-76-6P 494823-77-7P 494823-78-8P
494823-79-9P 494823-80-2P 494823-81-3P
494823-82-4P 494823-83-5P 494823-84-6P
494823-85-7P 494823-86-8P 494823-87-9P
494823-88-0P 494823-89-1P 494823-90-4P
494823-91-5P 494823-92-6P 494823-93-7P
494823-94-8P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; production of **acylated** polypeptides by recombinant expression of precursor proteins followed by **acylation** at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)

RN 106612-94-6 HCAPLUS

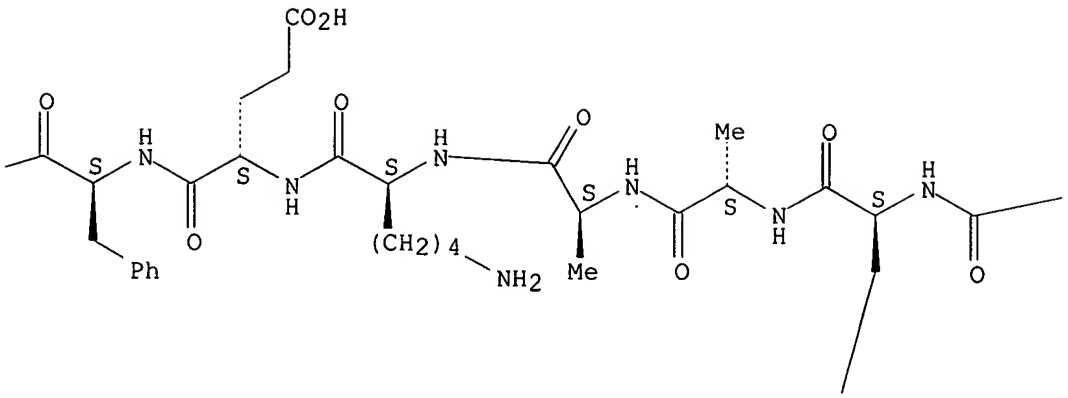
CN 7-37-Glucagon-like peptide I (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

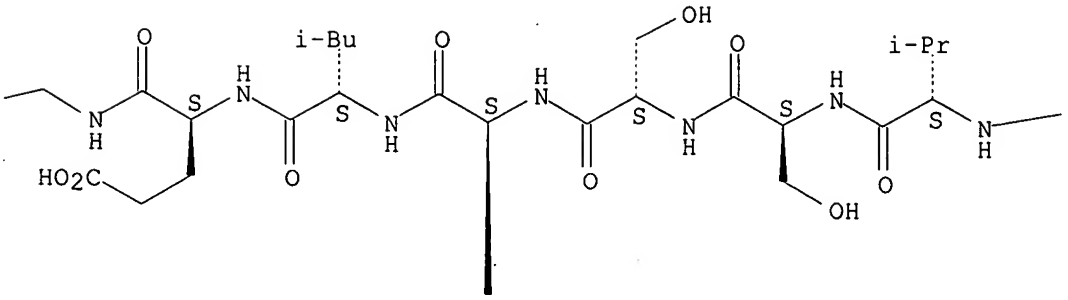
PAGE 1-A



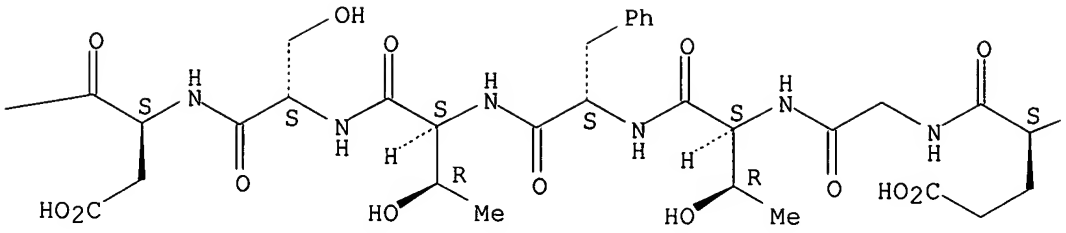
PAGE 1-B



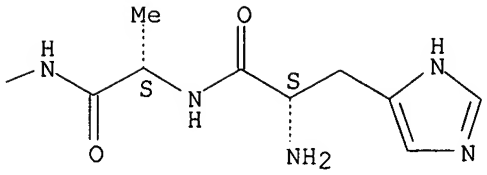
PAGE 1-C



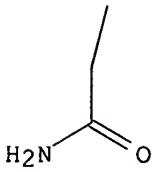
PAGE 1-D



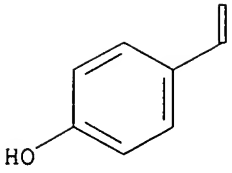
PAGE 1-E



PAGE 2-B



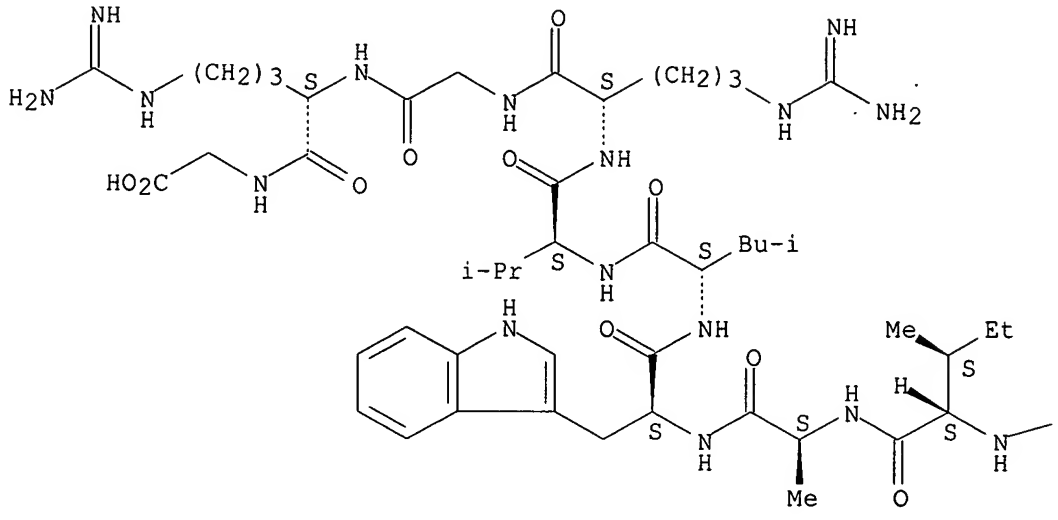
PAGE 2-C



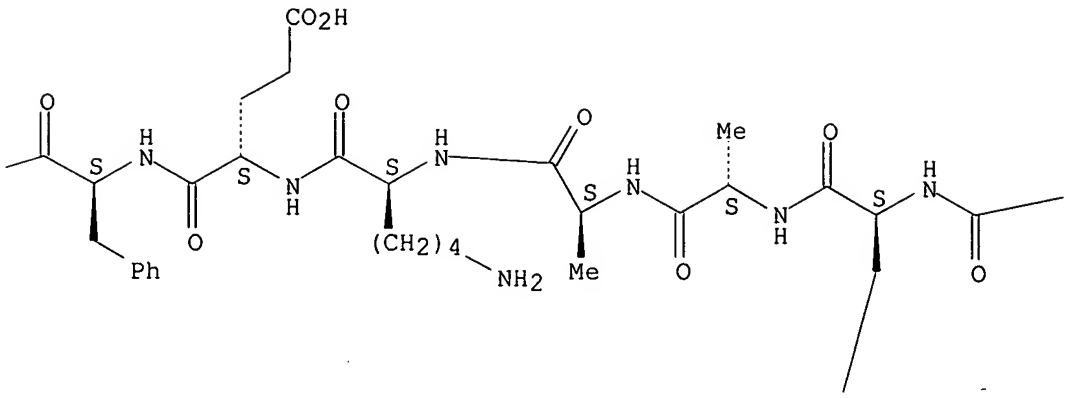
RN 204521-68-6 HCAPLUS
CN 7-36-Glucagon-like peptide 1 (Octodon degus), 34-L-arginine-36a-glycine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

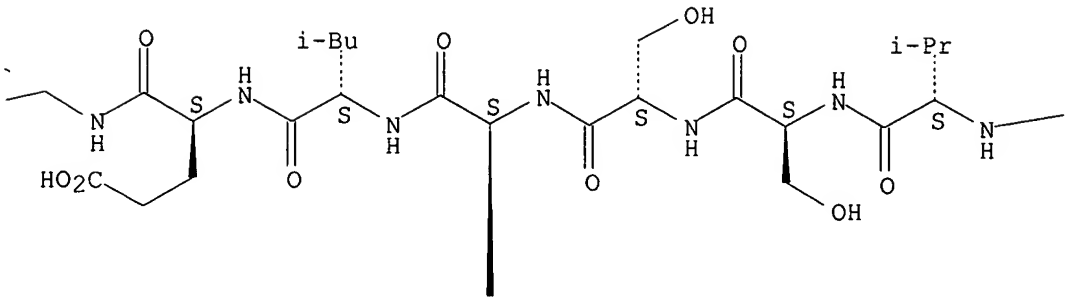
PAGE 1-A



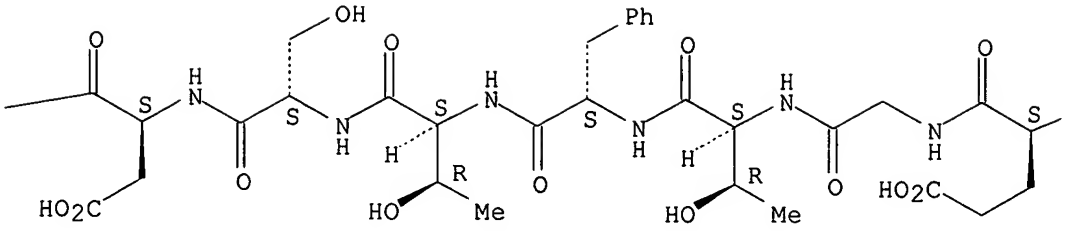
PAGE 1-B



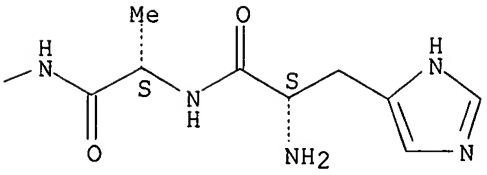
PAGE 1-C



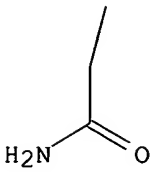
PAGE 1-D



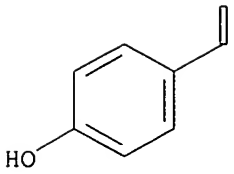
PAGE 1-E



PAGE 2-B



PAGE 2-C



RN 494823-59-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-60-8 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-61-9 HCAPLUS
CN Glycine, L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-62-0 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-63-1 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-

L-alanyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-64-2 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-65-3 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-66-4 HCAPLUS
CN Glycine, L-α-glutamyl-L-histidyl-L-prolyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-67-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-α-glutamyl-L-prolyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-68-6 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-histidyl-L-cysteinyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-69-7 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-histidyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-

L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-70-0 HCAPLUS
CN Glycine, L-α-glutamyl-L-histidyl-L-histidyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-71-1 HCAPLUS
CN Glycine, L-α-glutamyl-L-histidyl-L-alanyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-72-2 HCAPLUS
CN Glycine, L-α-glutamylglycyl-L-alanyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-73-3 HCAPLUS
CN Glycine, L-α-glutamyl-L-histidylglycyl-L-histidylglycyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-74-4 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-75-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-isoleucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-76-6 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-valyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-77-7 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-methionyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-78-8 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-phenylalanyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-79-9 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-tyrosyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-80-2 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-histidyl-L-α-glutamyl-L-tryptophyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-81-3 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-asparaginyl-L-threonyl-L-threonyl-L-prolyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-82-4 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-asparaginyl-L-α-glutamyl-L-threonyl-L-α-glutamyl-L-prolyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-83-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-asparaginyl-L-α-aspartyl-L-threonyl-L-α-glutamyl-L-prolyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-84-6 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-asparaginyl-L-threonyl-L-threonyl-L-α-glutamyl-L-prolyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-85-7 HCAPLUS
CN Glycine, L-glutaminyl-L-α-aspartyl-L-alanyl-L-histidyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-86-8 HCAPLUS
CN Glycine, L-glutaminyl-L-α-aspartyl-L-threonyl-L-alanyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-87-9 HCAPLUS
CN Glycine, L-α-aspartyl-L-α-aspartyl-L-α-aspartyl-L-α-aspartyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 494823-88-0 HCAPLUS
CN Glycine, L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-tryptophyl-L-histidyl-L-tryptophyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-89-1 HCAPLUS
CN Glycine, L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-tryptophyl-L-histidyl-L-tryptophyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-90-4 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-tryptophyl-L-histidyl-L-tryptophyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-91-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-α-glutamyl-L-alanyl-L-tryptophyl-L-histidyl-L-tryptophyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-92-6 HCAPLUS
CN Glycine, L-leucyl-L-α-aspartylglycyl-L-arginyl-L-leucyl-L-α-glutamyl-L-alanyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-93-7 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-leucyl-L-α-aspartylglycyl-L-arginyl-L-leucyl-L-α-glutamyl-L-alanyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-94-8 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-leucyl-L-α-aspartyl-L-alanyl-L-arginyl-L-leucyl-L-α-glutamyl-L-alanyl-L-leucyl-L-lysyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **89750-14-1P**, Glucagon-like peptide I **89750-15-2P**, Glucagon-like peptide II
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(production of **acylated** polypeptides by recombinant expression of precursor proteins followed by **acylation** at the lysine ε-amino groups and proteolytic cleavage of the N-terminal extension)
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 89750-15-2 HCAPLUS
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:97434 HCAPLUS
DN 138:149945
ED Entered STN: 07 Feb 2003
TI Production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage
IN Balschmidt, Per; Diers, Ivan; Egel-Mitani, Michi; Markussen, Jan; Hoeg-Jensen, Thomas
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K0001-00
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 3, 6
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003010185	A2	20030206	WO 2002-DK501	20020718
	WO 2003010185	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	EP 1421102	A2	20040526	EP 2002-750841	20020718
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005503141	T2	20050203	JP 2003-515544	20020718
	US 2003082671	A1	20030501	US 2002-205270	20020724
	US 2005272125	A1	20051208	US 2005-191574	20050728
PRAI	DK 2001-1140	A	20010724		
	US 2001-310952P	P	20010808		
	WO 2002-DK501	W	20020718		
	US 2002-205270	A1	20020724		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003010185	ICM	C07K0001-00
	IPCI	C07K0001-00 [ICM,7]
	IPCR	C07K0001-00 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-605 [I,A]
	ECLA	C07K001/00B; C07K001/107D4; C07K014/605
EP 1421102	IPCI	C07K0001-00 [ICM,7]; C07K0014-605 [ICS,7]
	IPCR	C07K0001-00 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-605 [I,A]
JP 2005503141	IPCI	C12P0021-02 [ICM]; C07K0014-00 [ICS]; C12N0015-09 [ICS]; C12R0001-865 [ICS]
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US 2003082671	IPCI	C12P0021-06 [ICM,7]
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	NCL	435/068.100
	ECLA	C07K001/00B; C07K001/107D4; C07K014/605
US 2005272125	IPCI	C12P0021-06 [ICM,7]; C07H0021-04 [ICS,7]; C07K0014-605 [ICS,7]
	NCL	435/069.100; 435/320.100; 435/325.000; 530/397.000; 536/023.500
	ECLA	C07K001/00B; C07K001/107D4; C07K014/605

OS MARPAT 138:149945

AB The present invention is related to a method of producing polypeptides in transformed host cells by expressing a precursor mol. of the desired polypeptide which is to be acylated in a subsequent in vitro step, preferentially in certain lysine ε-amino groups. The invention is also related to DNA sequences, vectors, and transformed host cells for use in the claimed method. Further, the present invention is related to certain precursors of the desired polypeptides and certain acylation methods. The precursor comprises N-terminal extensions which can by cleaved after acylation by enzymic proteolytic degradation Thus, Glu-Glu-Ala-Glu-Asn-Arg34glucagon-like peptide I(7-37) is expressed in yeast, acylated in position Lys-26 in a yield of 80% by Nε-palmitoyl-Glu-γ-succinimidyl-α-tert-Bu ester, and deprotected by use of TFA, and cleaved by hydroxylamine. Other specific N-terminal extensions are exemplified for cleavage with blood-coagulation factor Xa, kexin, and prolyl endopeptidase from Sphingomonas capsulata.

ST protein acylation precursor cloning proteolysis; glucagon like peptide I acylation precursor proteolysis

IT **Acylation**

Molecular cloning
(production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT Proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT Saccharomyces cerevisiae
Yeast
(recombinant expression host; production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT 730-08-5 2578-58-7 16874-75-2 78603-76-6 494847-25-5 494847-26-6 494847-27-7 494847-28-8 494847-29-9 494847-30-2 494847-31-3 494847-32-4 494847-33-5 494847-34-6 494847-35-7 494847-36-8 494847-37-9 494847-38-0
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(N-terminal extension; production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT **204521-63-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation reagent; production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT **204521-68-6P 494823-11-9P 494823-12-0P 494823-13-1P 494823-14-2P 494823-15-3P 494823-16-4P 494823-17-5P 494823-18-6P 494823-19-7P 494823-20-0P 494823-21-1P 494823-22-2P 494823-23-3P 494823-24-4P 494823-25-5P 496044-36-1P**
RL: BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; production of **acylated** polypeptides by recombinant preparation of precursor proteins followed by **acylation** of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT 7803-49-8, Hydroxylamine, uses 9002-05-5, Blood-coagulation factor Xa 72162-84-6, Prolyl endopeptidase 99676-46-7, Kexin
RL: CAT (Catalyst use); USES (Uses)
(cleavage reagent; production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

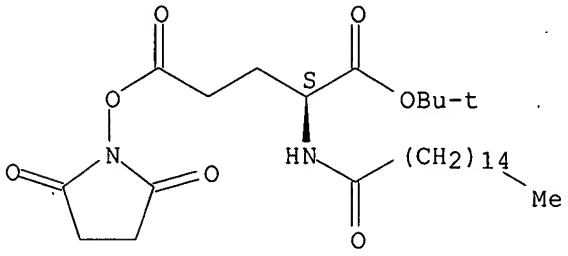
IT 9034-39-3P, Growth hormone-releasing hormone **89750-14-1P**, Glucagon-related peptide I **89750-15-2P**, Glucagon-related peptide II
RL: BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(production of **acylated** polypeptides by recombinant preparation of precursor proteins followed by **acylation** of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT 56-87-1, L-Lysine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

IT **204521-63-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation reagent; production of acylated polypeptides by recombinant preparation of precursor proteins followed by acylation of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

RN 204521-63-1 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-2-[(1-oxohexadecyl)amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

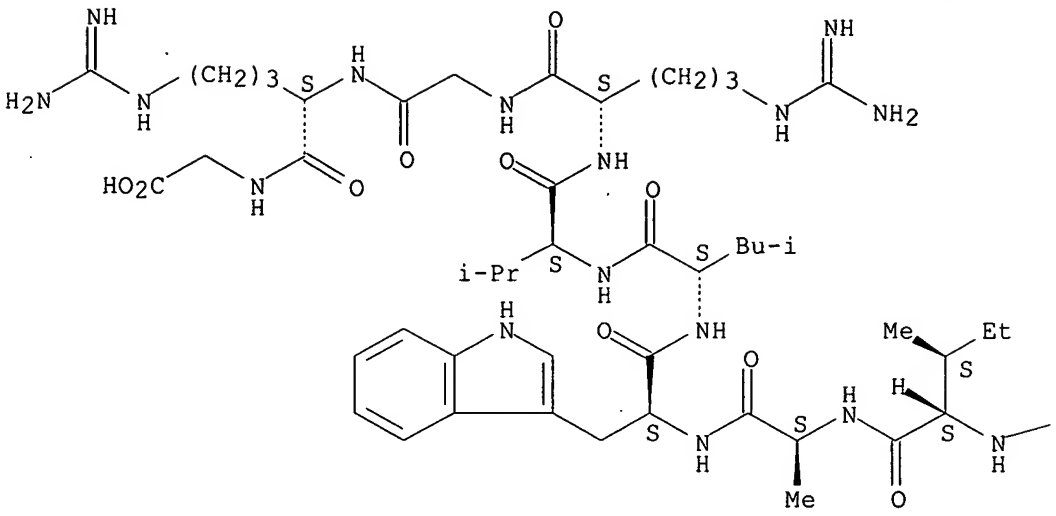


IT **204521-68-6P 494823-11-9P 494823-12-0P**
494823-13-1P 494823-14-2P 494823-15-3P
494823-16-4P 494823-17-5P 494823-18-6P
494823-19-7P 494823-20-0P 494823-21-1P
494823-22-2P 494823-23-3P 494823-24-4P
494823-25-5P 496044-36-1P
RL: BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; production of **acylated** polypeptides by recombinant preparation of precursor proteins followed by **acylation** of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)

RN 204521-68-6 HCAPLUS
CN 7-36-Glucagon-like peptide 1 (Octodon degus), 34-L-arginine-36a-glycine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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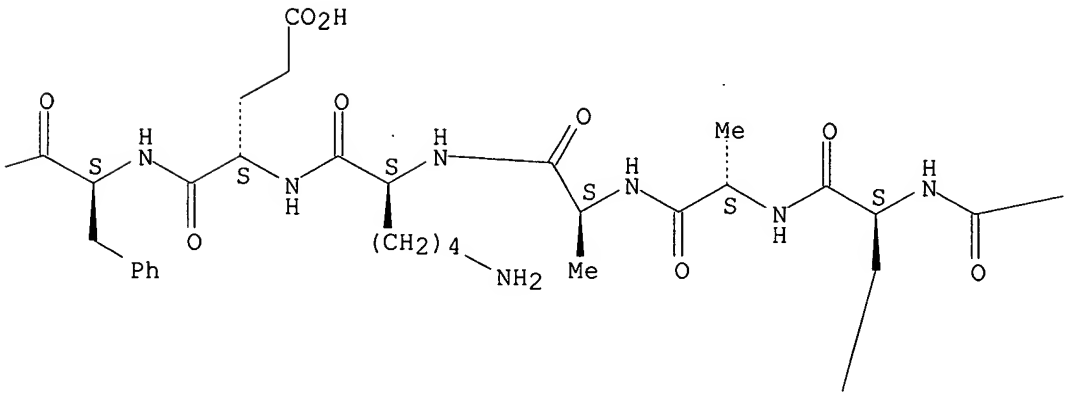

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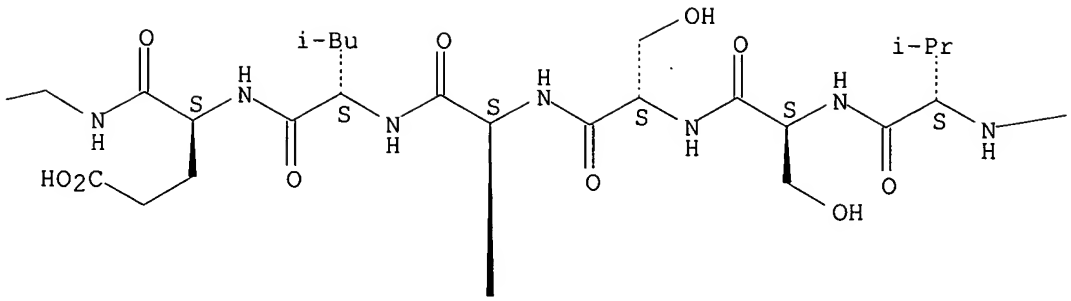

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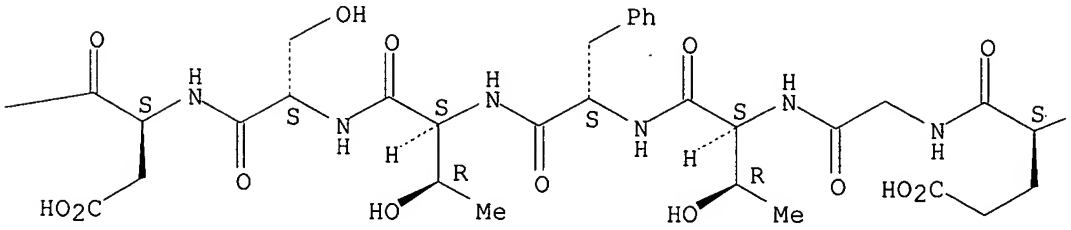

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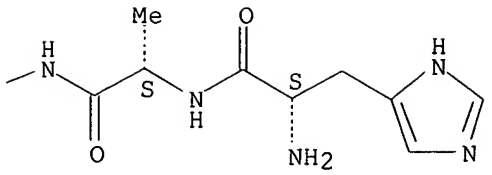

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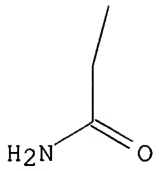

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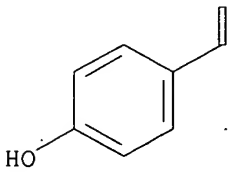

RN 494823-11-9 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-methionyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-12-0 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-methionyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-

L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-13-1 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-asparaginyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-14-2 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-arginyl-L-arginyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-15-3 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-arginyl-L-alanyl-L-arginyl-L-arginyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-16-4 HCAPLUS
CN Glycine, L-α-glutamyl-L-prolyl-L-glutaminyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-17-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-alanyl-L-glutaminyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-18-6 HCAPLUS
CN Glycine, L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-glutaminyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-

tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

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RN 494823-19-7 HCAPLUS
CN Glycine, L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-alanyl-L-glutaminyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-20-0 HCAPLUS
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-21-1 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamylglycyl-L-α-glutamyl-L-prolyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-22-2 HCAPLUS
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-23-3 HCAPLUS
CN Glycine, L-α-glutamyl-L-histidylglycyl-L-cysteinyl-L-threonyl-L-seryl-L-isoleucyl-L-cysteinyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-24-4 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-alanyl-L-α-glutamyl-L-cysteinyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-

tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 494823-25-5 HCAPLUS
CN Glycine, L-α-glutamyl-L-α-glutamyl-L-isoleucyl-L-α-glutamylglycyl-L-arginyl-L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 496044-36-1 HCAPLUS
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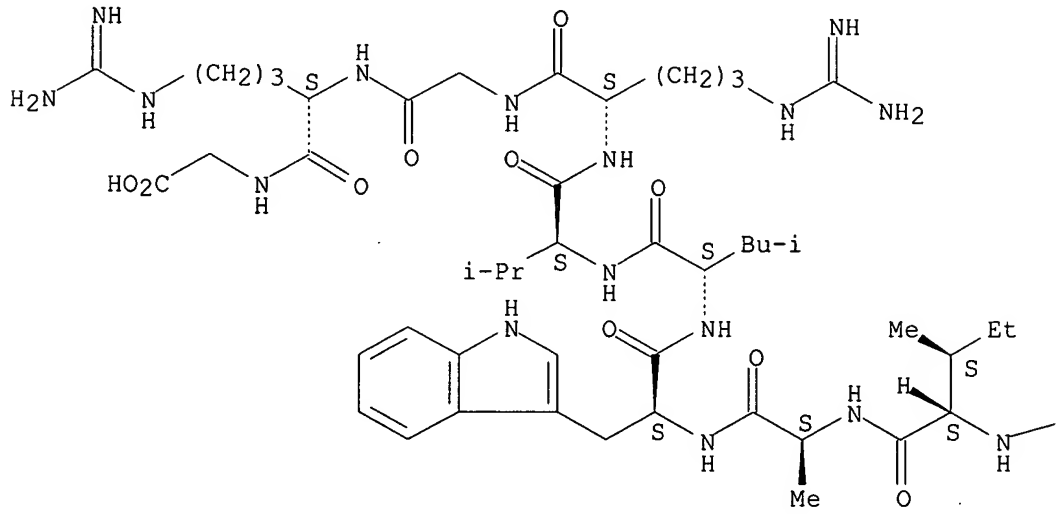
Absolute stereochemistry.

PAGE 1-A



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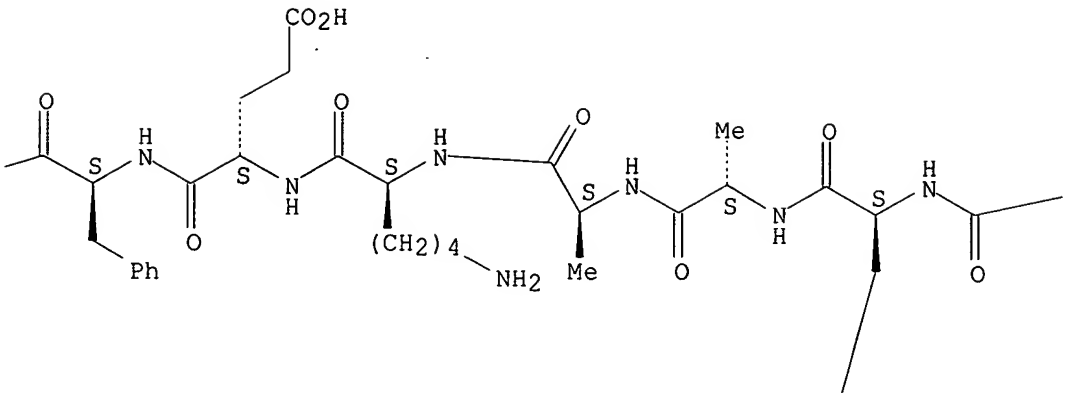

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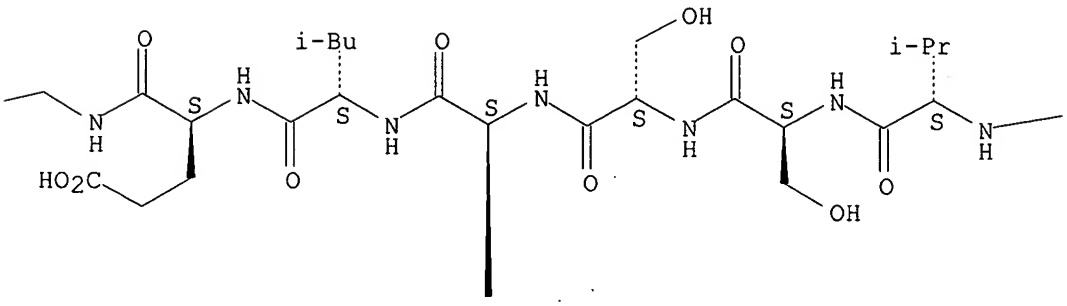

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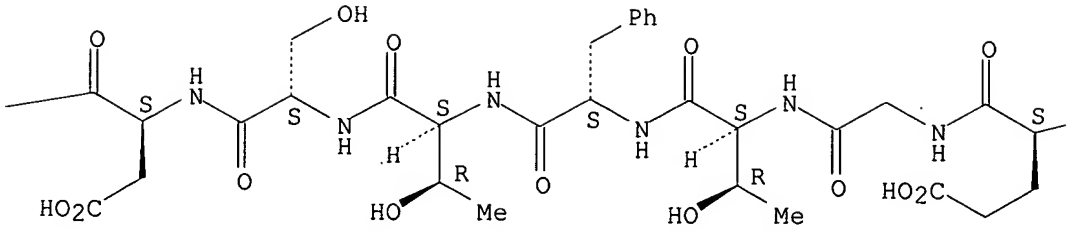

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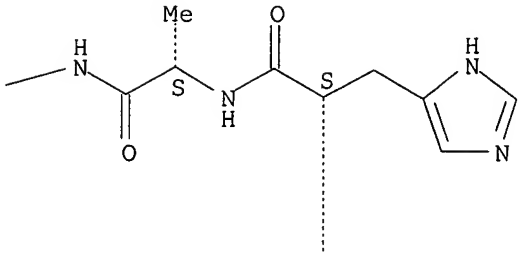

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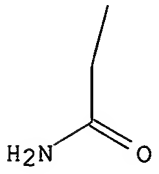

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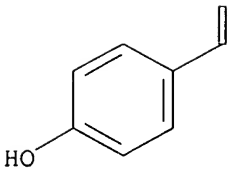

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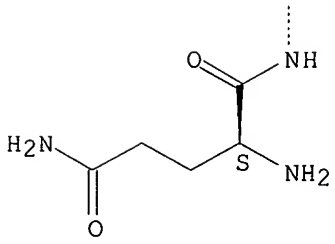

IT **89750-14-1P**, Glucagon-related peptide I **89750-15-2P**, Glucagon-related peptide II
RL: BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(production of **acylated** polypeptides by recombinant preparation of precursor proteins followed by **acylation** of the precursor protein on lysine ε-amino groups and subsequent proteolytic cleavage)
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 89750-15-2 HCAPLUS
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:666694 HCAPLUS
DN 133:252749
ED Entered STN: 22 Sep 2000
TI Method for acylating peptides and novel acylating agents
IN **Hansen, Louis Brammer**
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C0235-72
ICS C07K0001-06
CC 34-3 (Amino Acids, Peptides, and Proteins)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000055119	A1	20000921	WO 2000-DK117	20000316
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	EP 1163211	A1	20011219	EP 2000-910573	20000316
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
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	NO 2001004508	A	20010917	NO 2001-4508	20010917
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	US 1999-126882P	P	19990330		
	WO 2000-DK117	W	20000316		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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	IPCI	C07C0235-72 [ICM,7]; C07K0001-06 [ICS,7]
	IPCR	C07D0207-00 [I,C]; C07D0207-46 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-605 [I,A]
	ECLA	C07D207/46; C07K001/107D4; C07K014/605
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	IPCR	C07D0207-00 [I,C]; C07D0207-46 [I,A]; C07K0001-00 [I,C]; C07K0001-107 [I,A]; C07K0014-435 [I,C]; C07K0014-605 [I,A]
	NCL	530/345.000; 436/086.000; 436/090.000; 530/308.000; 530/333.000; 530/402.000
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BR 2000009040	IPCI	C07C0235-72 [ICM,7]; C07K0001-06 [ICS,7]
EP 1163211	IPCI	C07C0235-72 [ICM,6]; C07K0001-06 [ICS,6]
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JP 2002539186	IPCI	C07D0207-46 [ICM,7]; C07K0001-08 [ICS,7]; C07B0061-00 [ICS,7]
ZA 2001006884	IPCI	C07C [ICM,7]; C07K [ICS,7]
NO 2001004508	IPCI	C07C0235-72 [ICM,7]; C07K0001-02 [ICS,7]

OS CASREACT 133:252749; MARPAT 133:252749
AB A method for acylating one or more amino groups of a peptide or protein

uses acylating agents R2CONHCH(CO2R1)(CH2)nCH2COR3 [n = 0-8; R1 = H, alkyl, benzyl; R2 is a lipophilic moiety; R3 together with the carboxyl group to which R3 is attached designate a reactive ester or a reactive N-hydroxy imide ester;] under basic conditions in a mixture of an aprotic polar solvent and water. Thus, Arg34Lys26-[N-ε-[γ-Glu(N-hexadecanoyl)]]-GLP-13-37 (GLP-1 = glucagon-like peptide-1) was prepared by acylation of Arg34-GLP-17-37 with N-hexadecanoylglutamic acid α-Me ester γ-N-hydroxysuccinimide ester followed by basic hydrolysis. The acylating agent was obtained by treating glutamic acid α-Me ester with 1-hexadecanoylbenzotriazole in N-methyl-2-pyrrolidone in the presence of triethylamine and conversion to the N-hydroxysuccinimide ester.

ST acylation peptide; GLP1 fragment acylation

IT **Acylation**
(method for acylating peptides)

IT **Peptides, reactions**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for **acylating** peptides)

IT **204656-20-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for acylating peptides)

IT 6384-08-3 13030-09-6 55889-33-3 **130391-54-7**, Exendin-3 **141732-76-5**, Exendin-4 **194551-05-8 204521-68-6** 204521-81-3 **213754-29-1 213754-31-5 213754-33-7 213754-35-9 224638-84-0 227472-22-2 258289-68-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for **acylating** peptides)

IT **73793-91-6P 294855-88-2P 294855-89-3P 294855-90-6P 294855-91-7P 294869-90-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for acylating peptides)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Kanji, M; Cehm Pharm Bull 1986, V34(7), P2840
(2) Miroshnikov, A; Zh Obshch Khim 1970, V40(2), P429 HCAPLUS
(3) Novo Nordisk AS; WO 9808871 A1 1998 HCAPLUS
(4) Novo Nordisk AS; WO 9808872 A1 1998 HCAPLUS

IT **204656-20-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for acylating peptides)

RN 204656-20-2 HCAPLUS

CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **130391-54-7**, Exendin-3 **141732-76-5**, Exendin-4 **194551-05-8 204521-68-6 213754-29-1 213754-31-5 213754-33-7 213754-35-9 224638-84-0 227472-22-2 258289-68-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for **acylating** peptides)

RN 130391-54-7 HCAPLUS

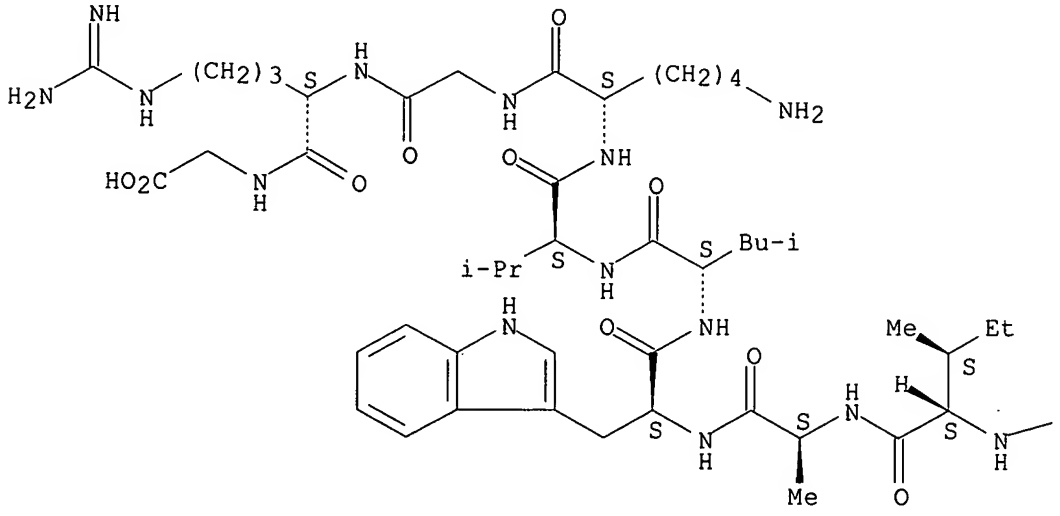
CN Exendin 3 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 141732-76-5 HCAPLUS
CN Exendin 4 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 194551-05-8 HCAPLUS
CN Glycine, L-histidyl-L-valyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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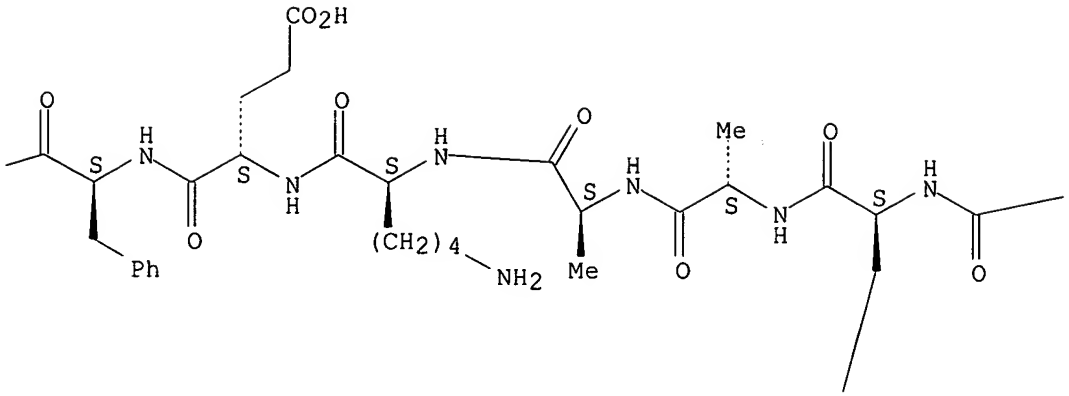

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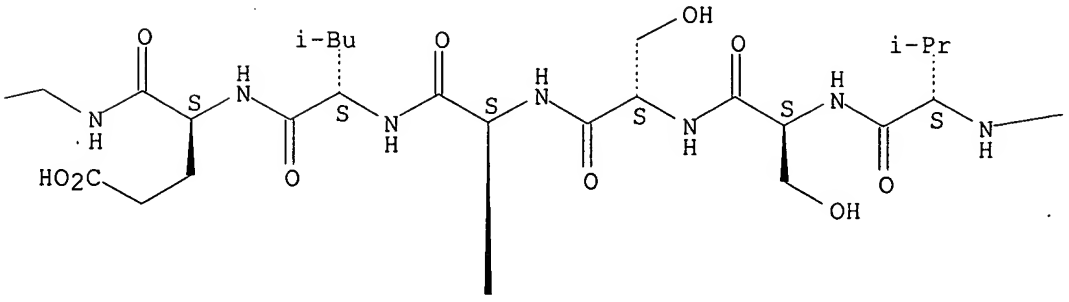

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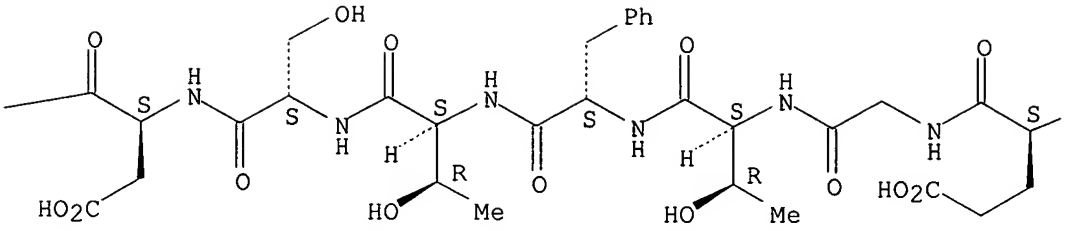

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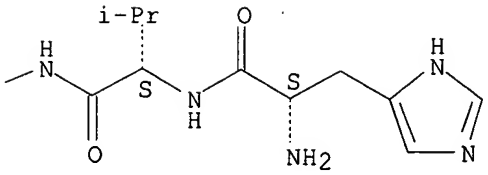

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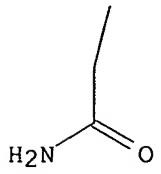

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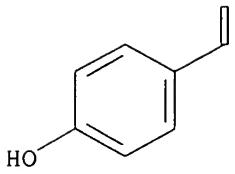

RN 204521-68-6 HCAPLUS
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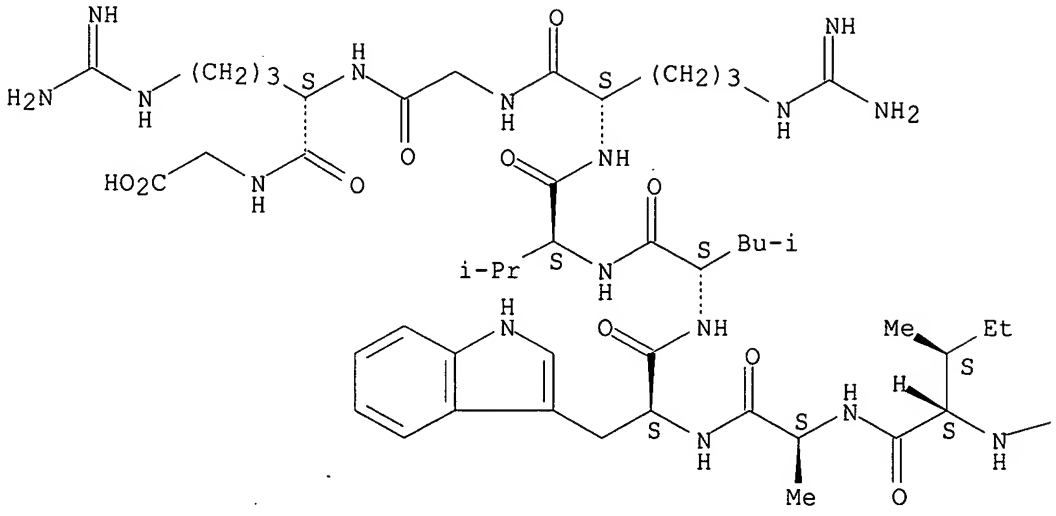
Absolute stereochemistry.

PAGE 1-A



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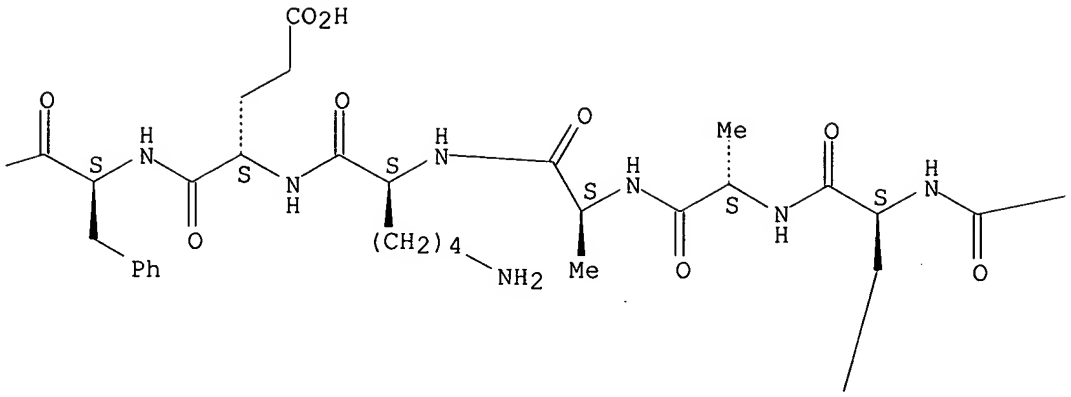

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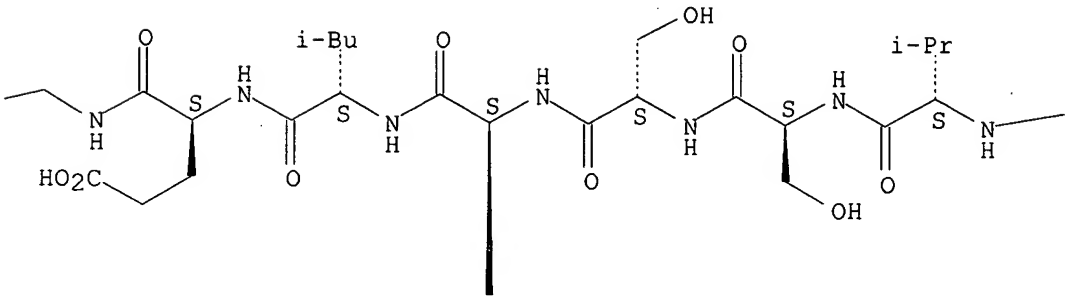

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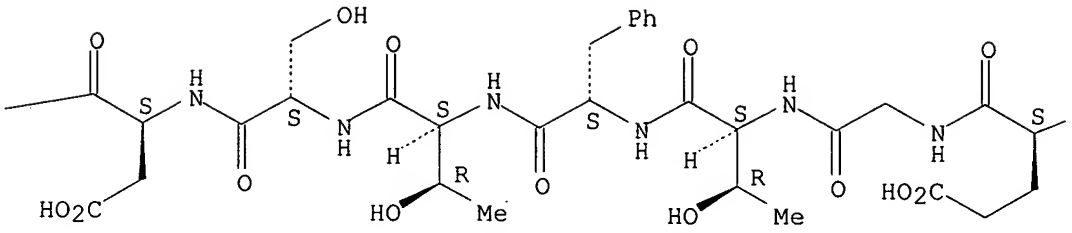

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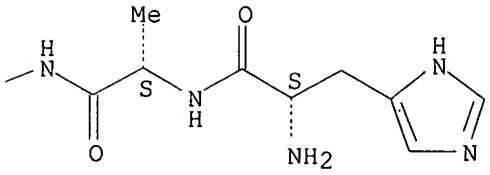

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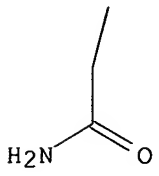

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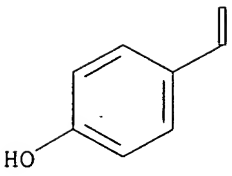
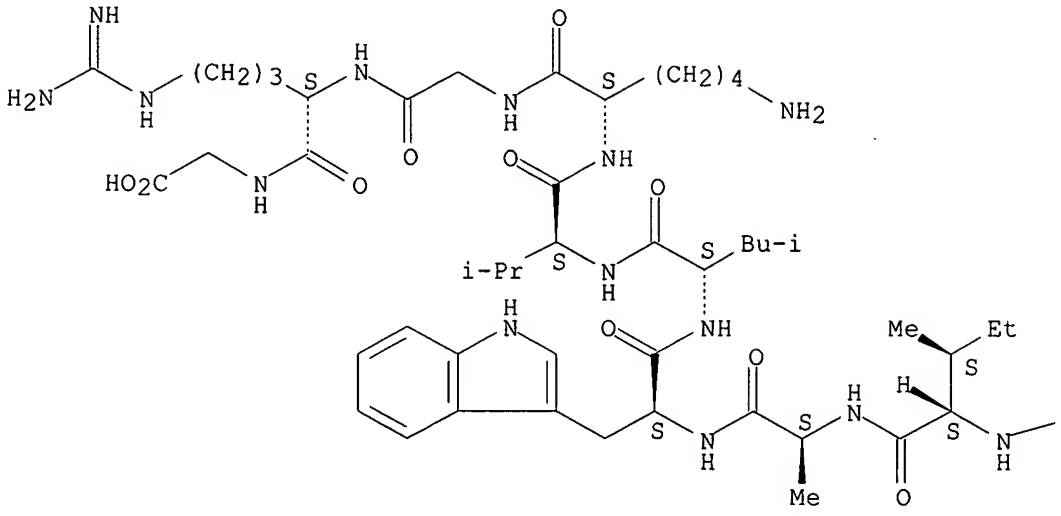


RN 213754-29-1 HCAPLUS
CN 7-37-Glucagon-like peptide I (human), 8-L-methionine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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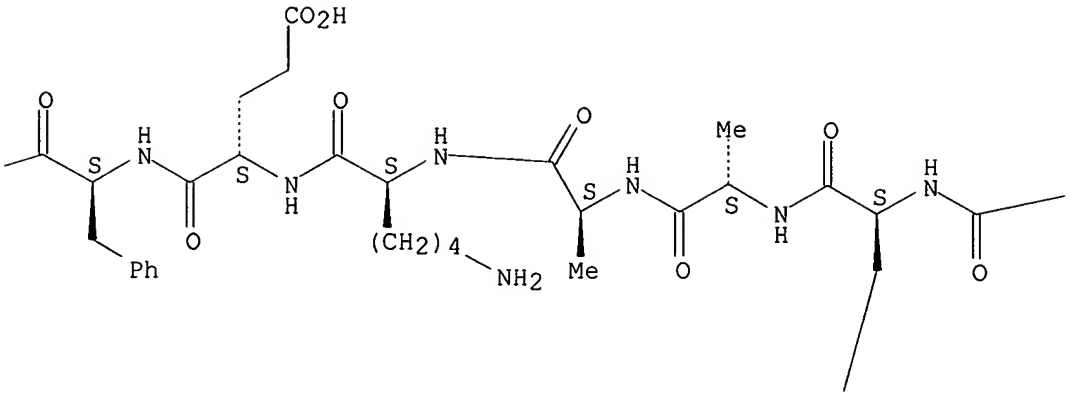

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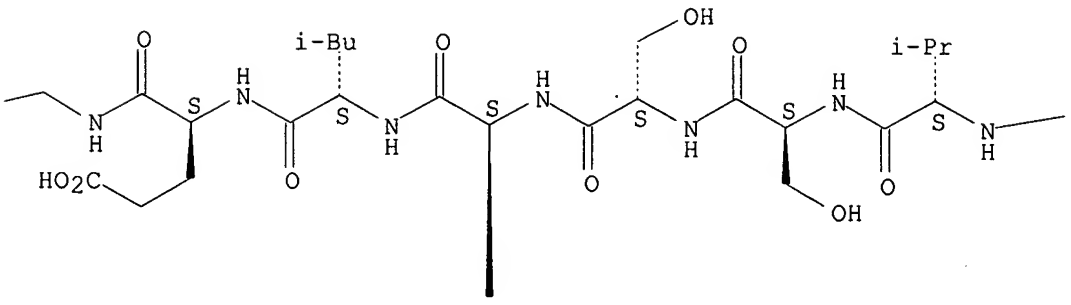

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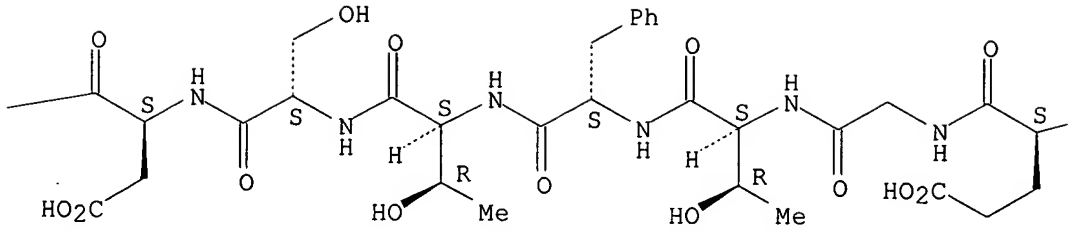

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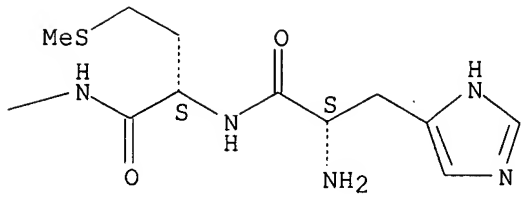

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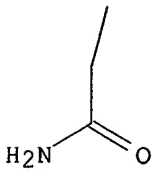

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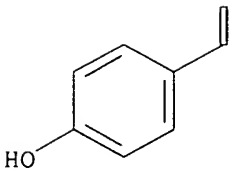
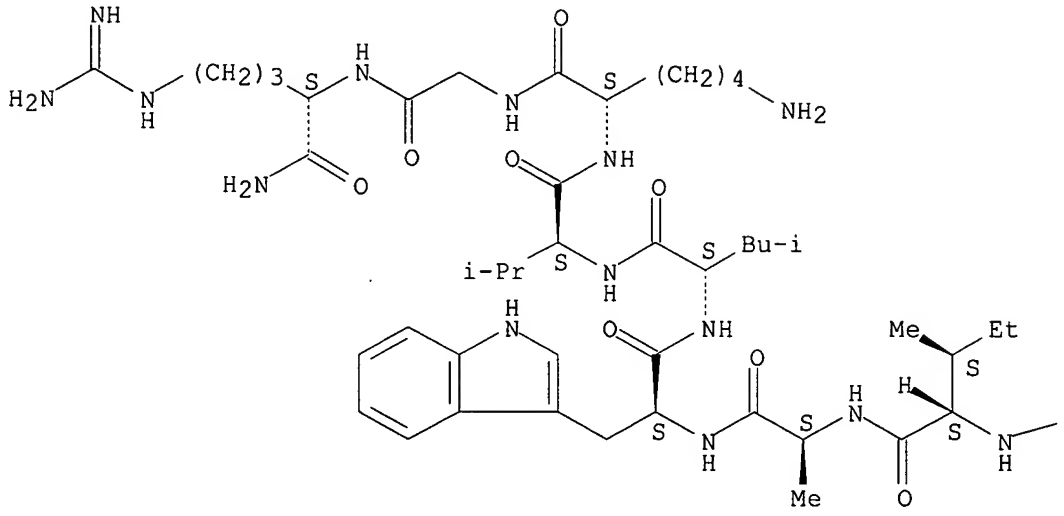


RN 213754-31-5 HCAPLUS
CN 7-36-Glucagon-like peptide I (human), 8-L-methionine-36-L-argininamide-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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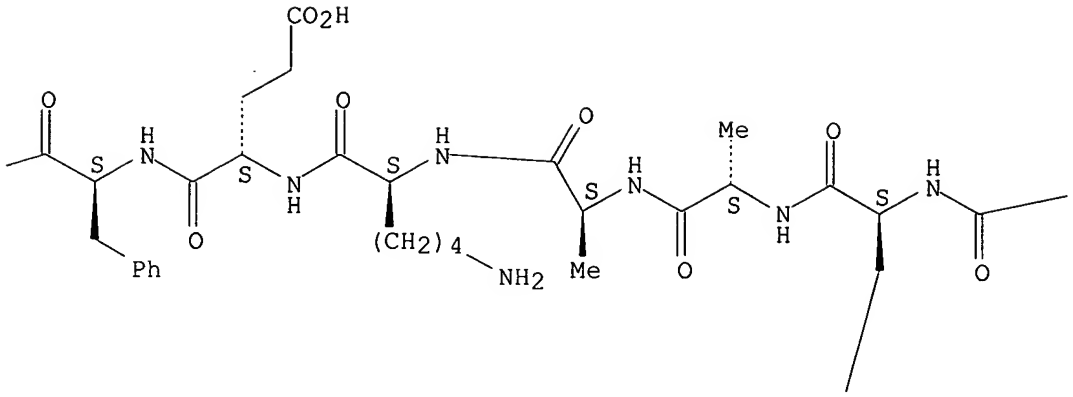

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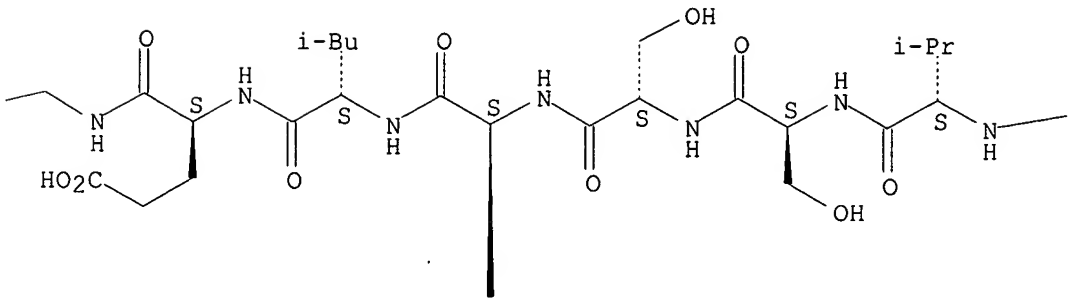

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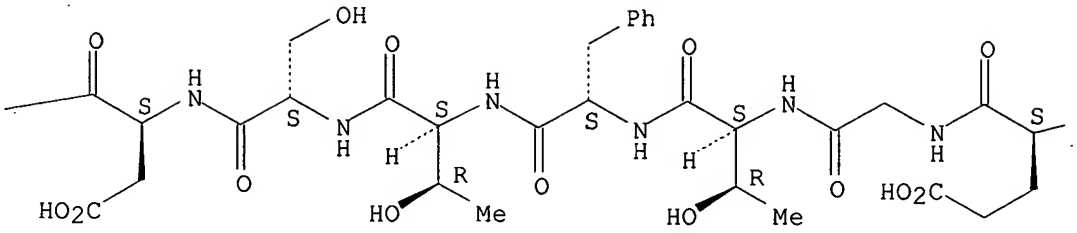

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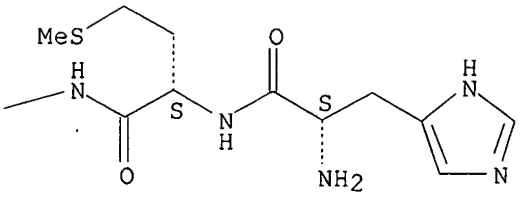

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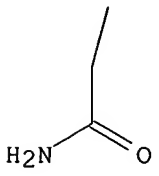

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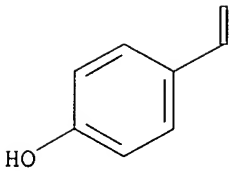
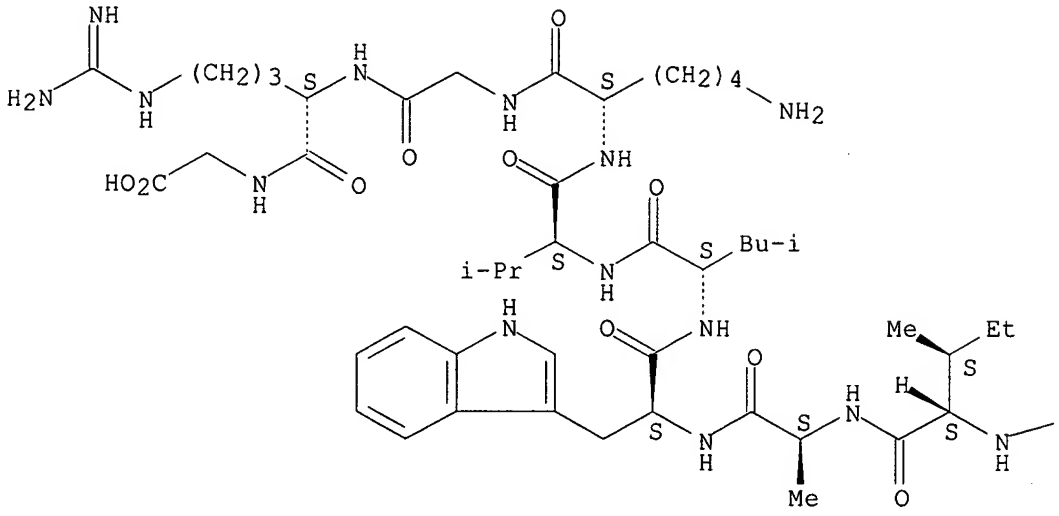


RN 213754-33-7 HCAPLUS
CN 7-37-Glucagon-like peptide I (human), 8-L-threonine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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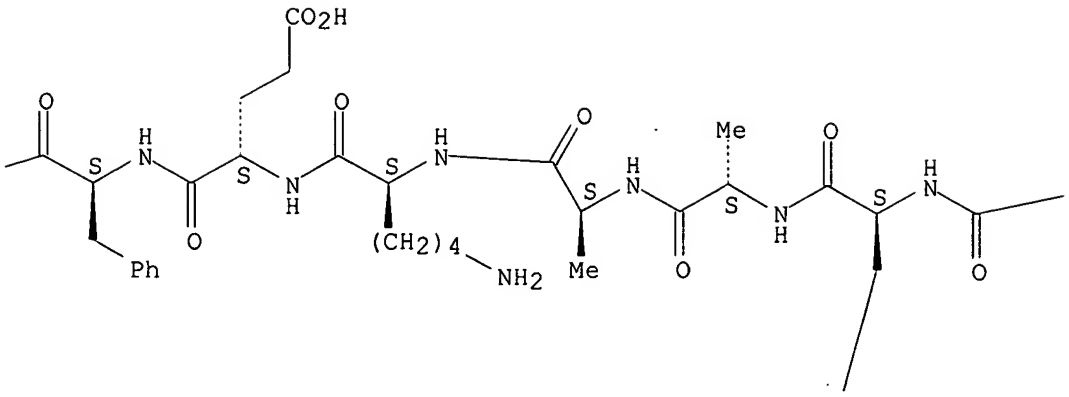

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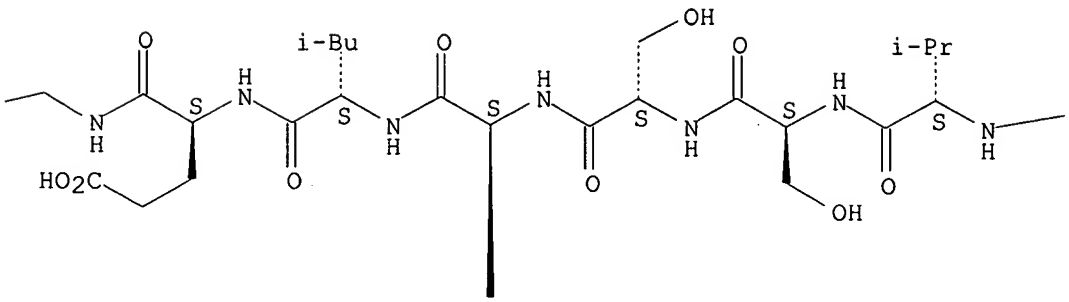

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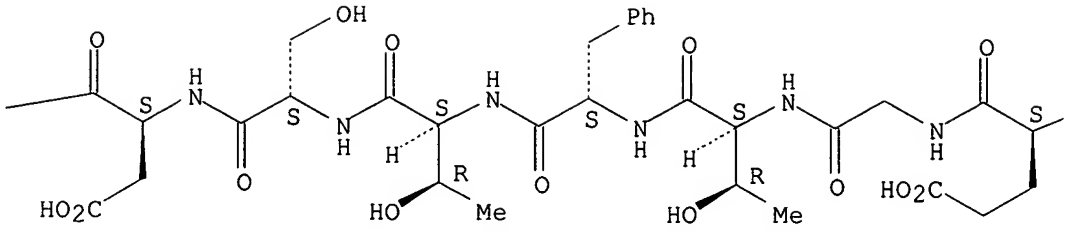

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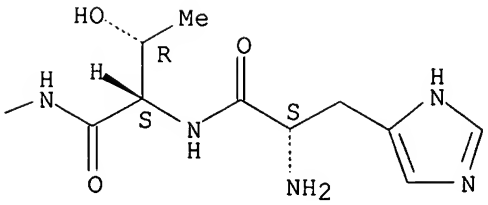

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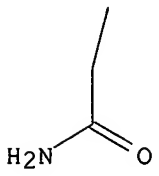

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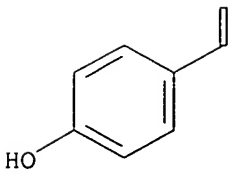
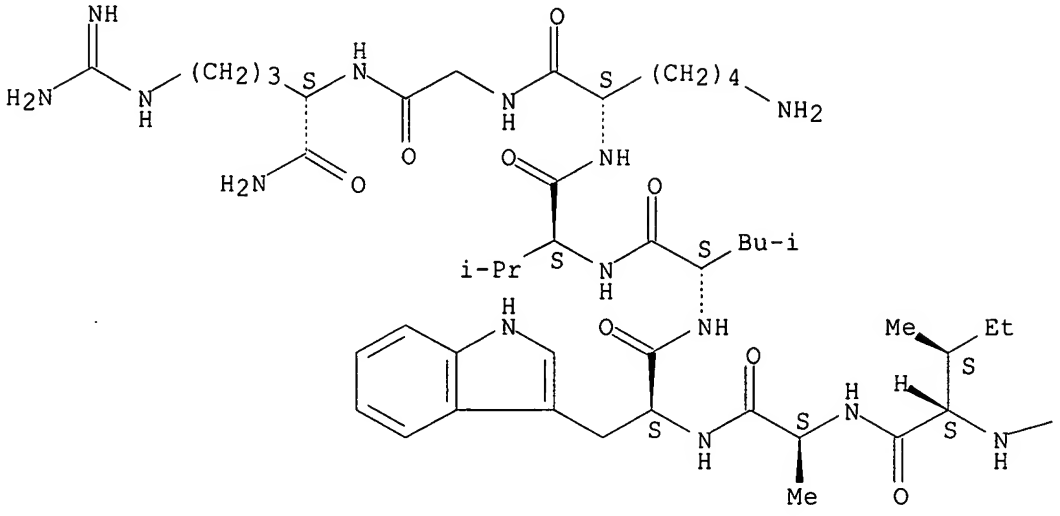


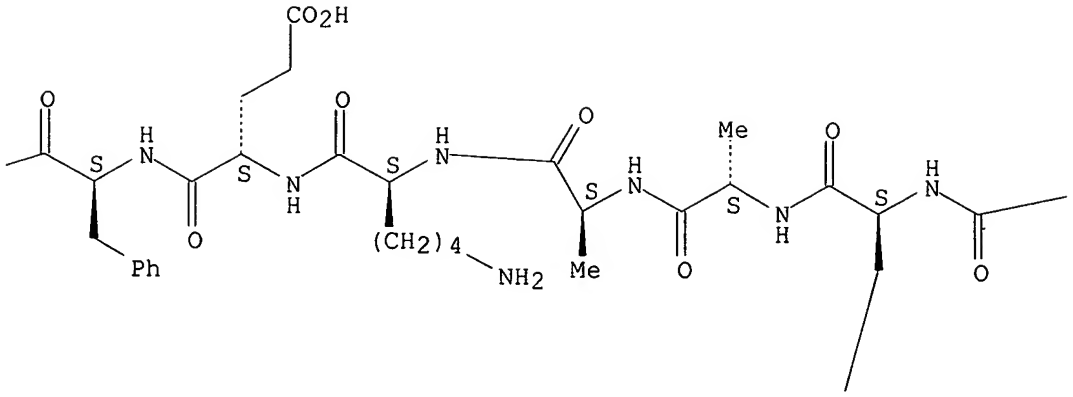
RN 213754-35-9 HCAPLUS
CN 7-36-Glucagon-like peptide I (human), 8-L-threonine-36-L-argininamide-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

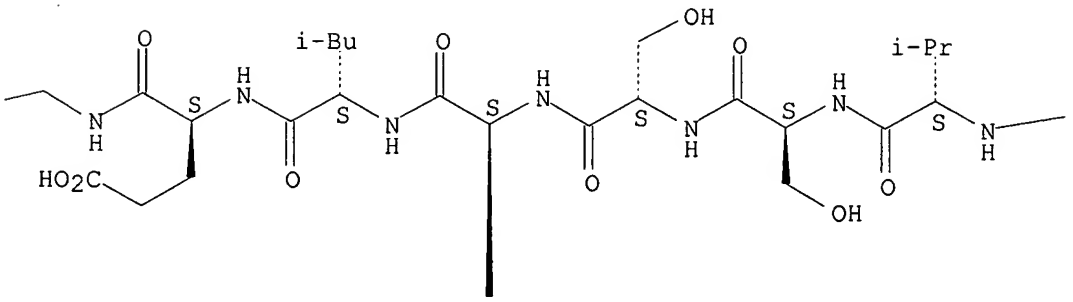
PAGE 1-A



PAGE 1-B



PAGE 1-C



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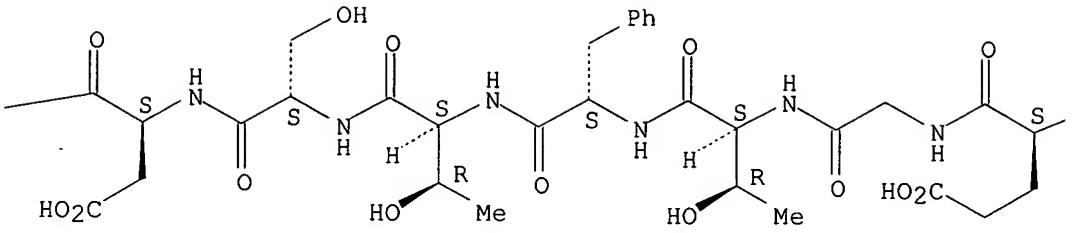
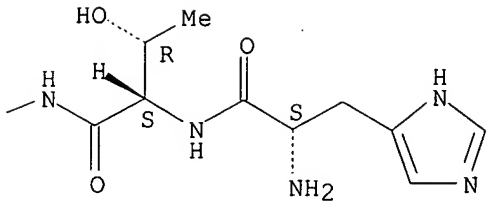


PAGE 1-E



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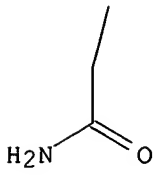

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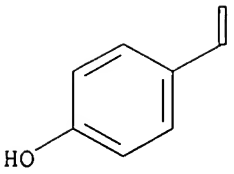
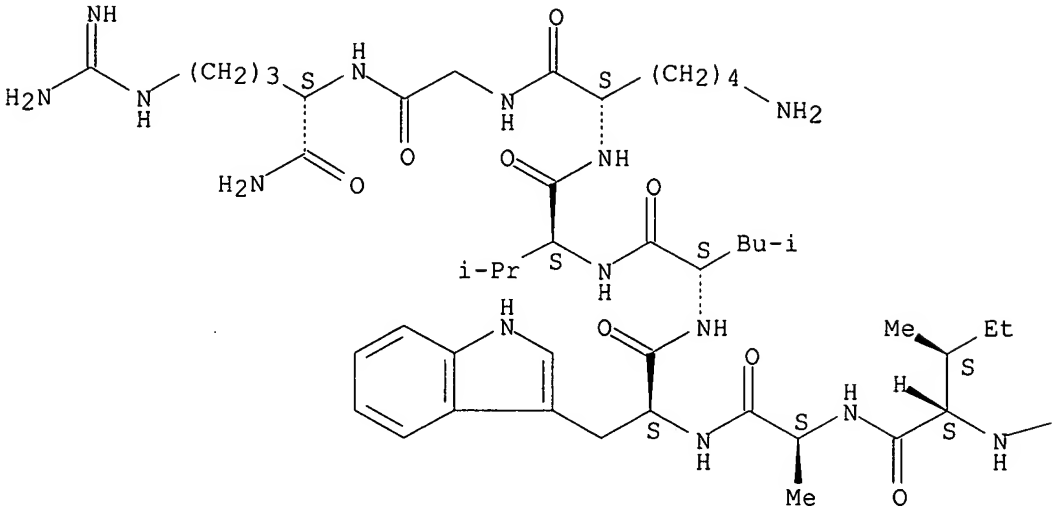


RN 224638-84-0 HCAPLUS
CN 7-36-Glucagon-like peptide 1 (Octodon degus), 8-glycine-36-L-argininamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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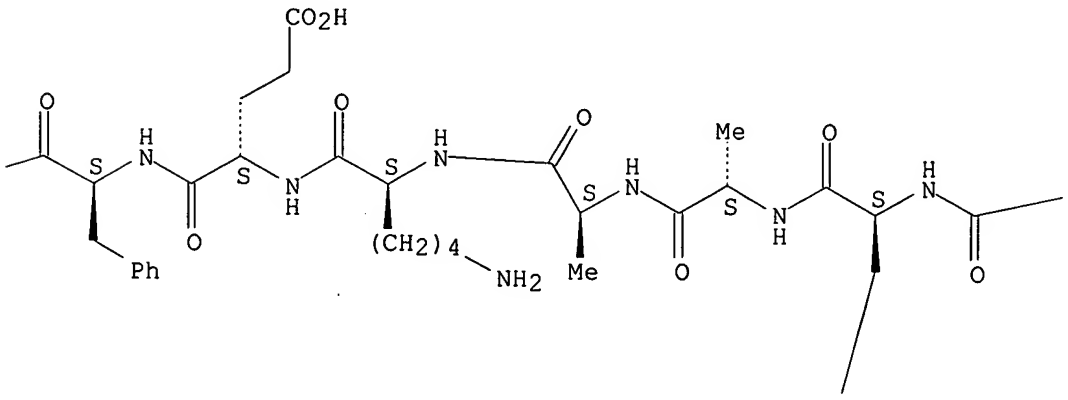
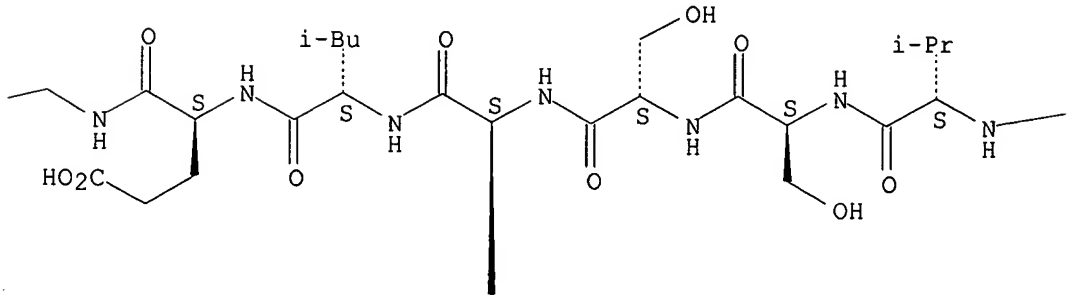


PAGE 1-C



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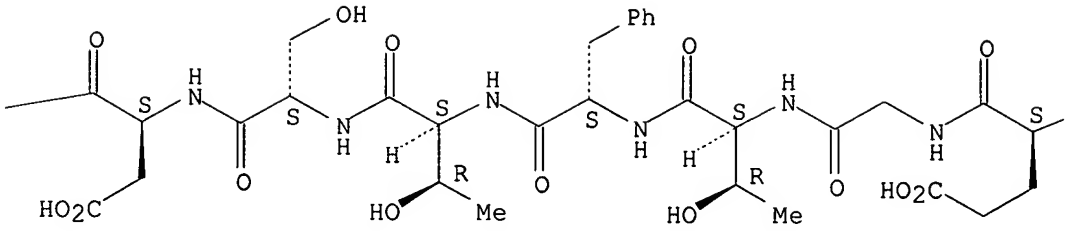

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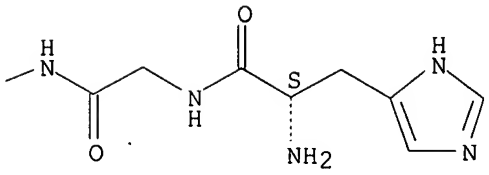

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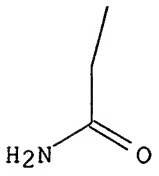

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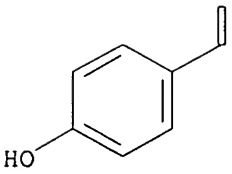
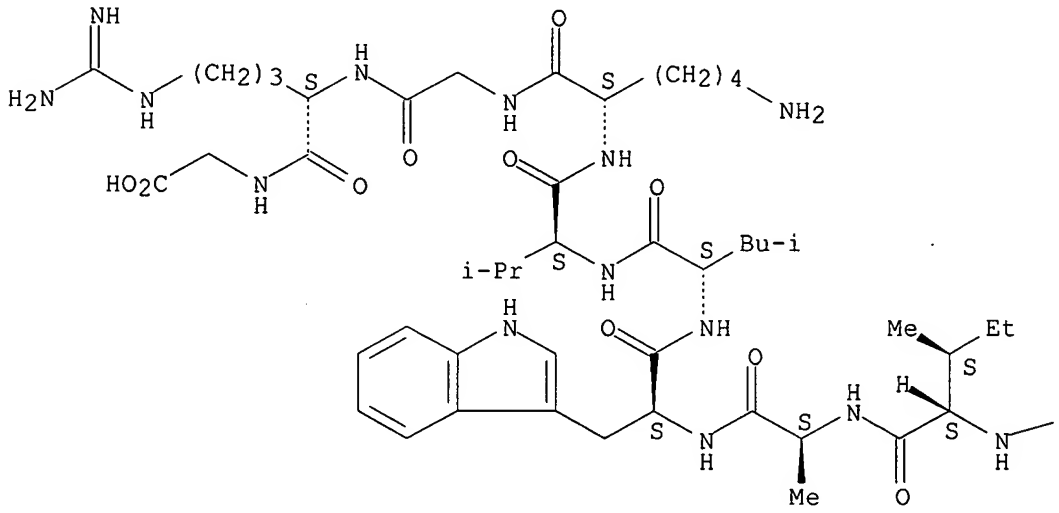


RN 227472-22-2 HCAPLUS
CN Glycine, L-histidylglycyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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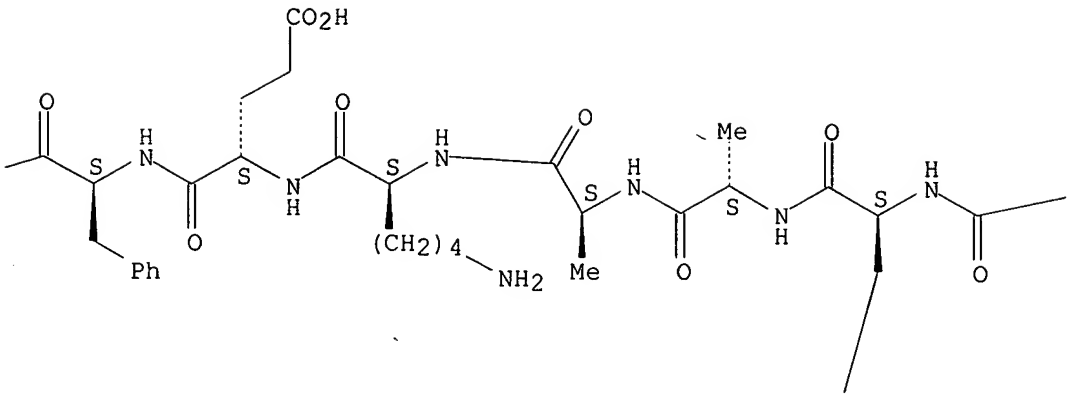

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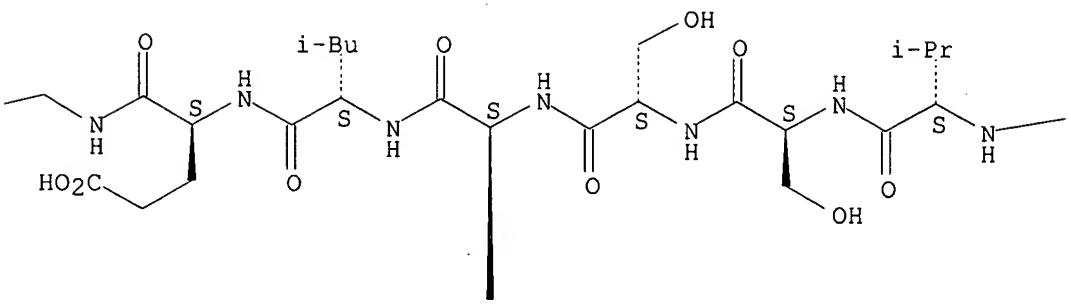
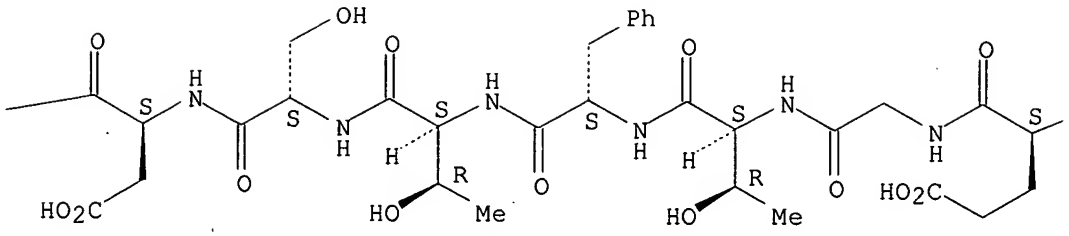


PAGE 1-D



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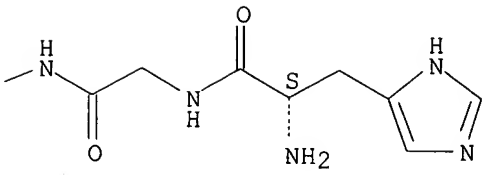

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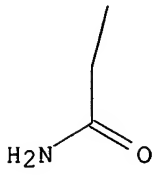

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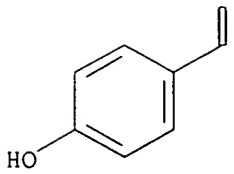
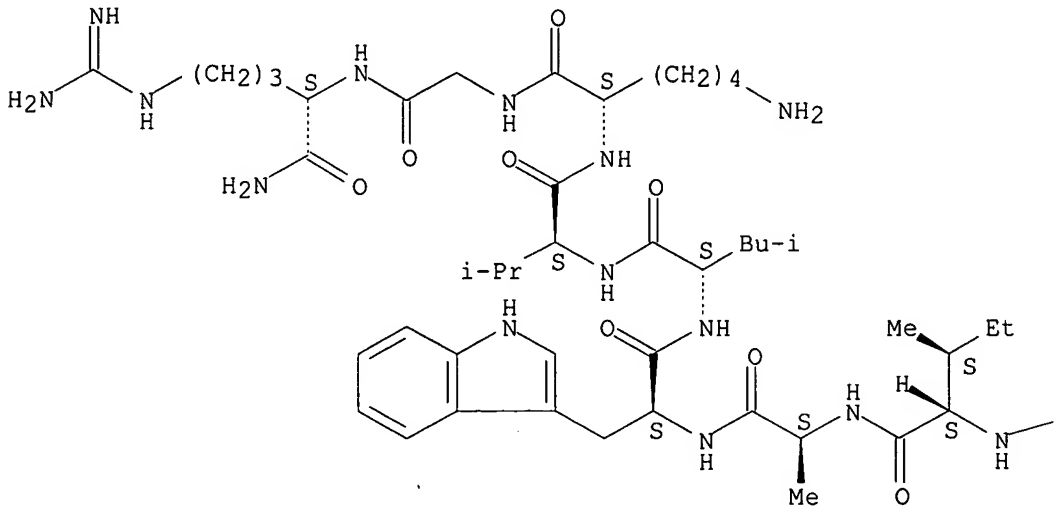


RN 258289-68-8 HCAPLUS
CN L-Argininamide, L-histidyl-L-valyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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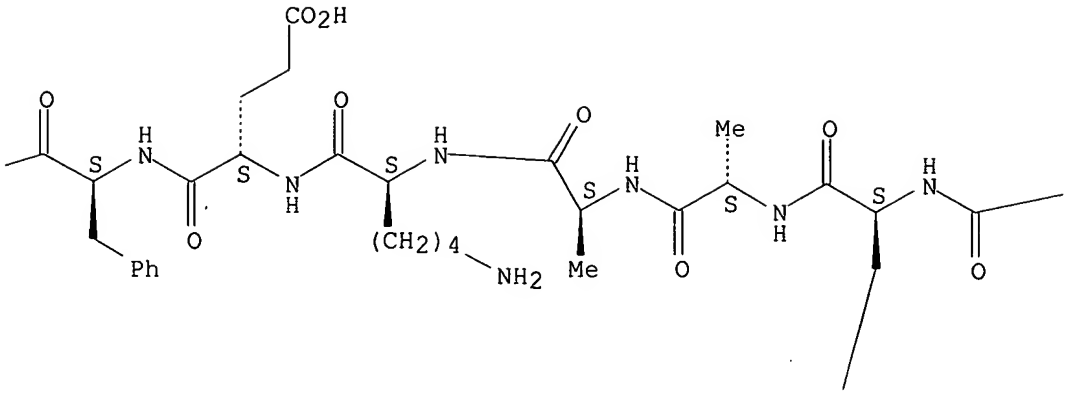
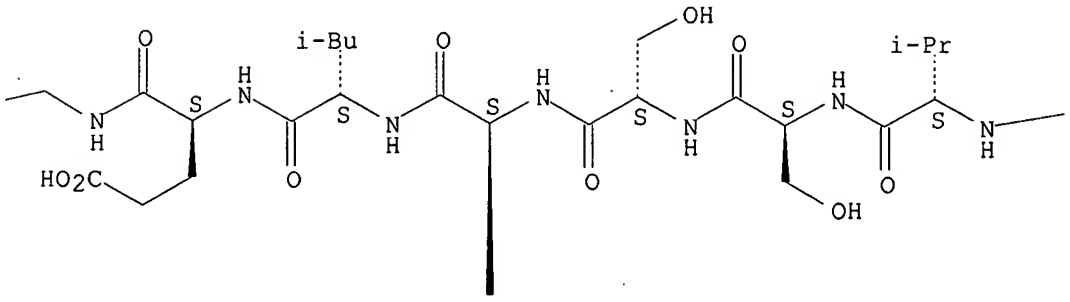


PAGE 1-C



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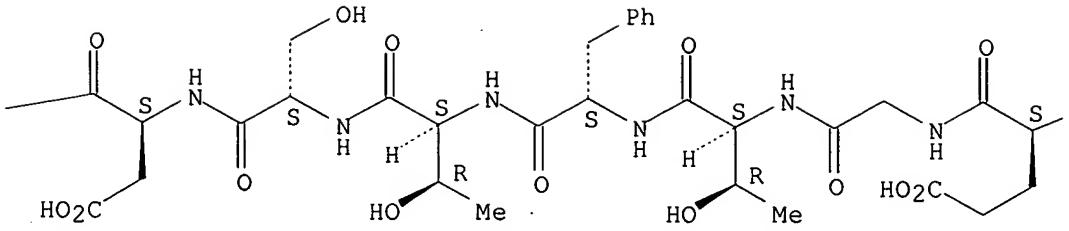

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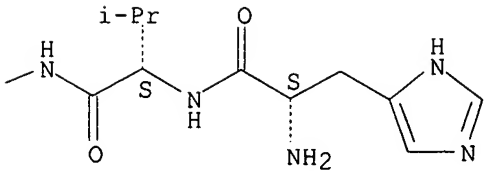

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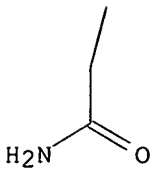

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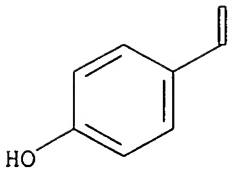
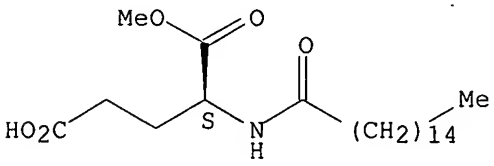


IT **73793-91-6P 294855-88-2P 294855-89-3P**
294855-90-6P 294855-91-7P 294869-90-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for acylating peptides)

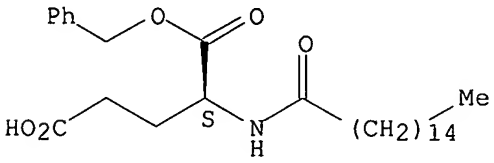
RN 73793-91-6 HCAPLUS
CN L-Glutamic acid, N-(1-oxohexadecyl)-, 1-methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



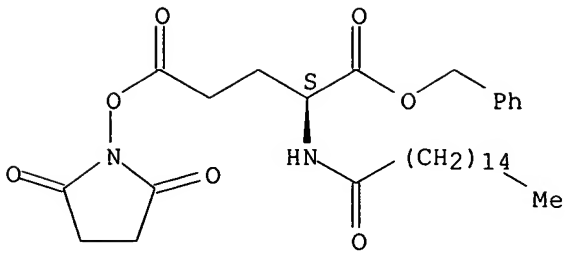
RN 294855-88-2 HCAPLUS
CN L-Glutamic acid, N-(1-oxohexadecyl)-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



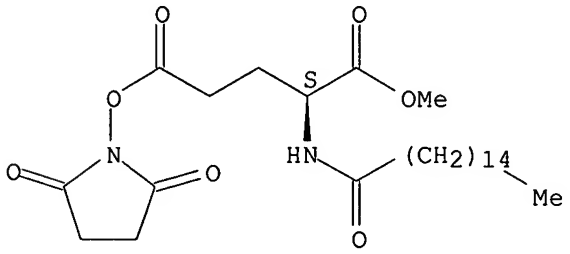
RN 294855-89-3 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-2-[(1-oxohexadecyl)amino]-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



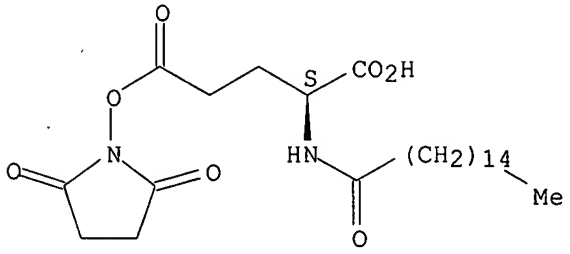
RN 294855-90-6 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-2-[(1-oxohexadecyl)amino]-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 294855-91-7 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-5-oxo-2-[(1-oxohexadecyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 294869-90-2 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[N-(1-oxohexadecyl)-L-γ-glutamyl]-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-arginylglycyl-L-arginyl-, 1'-methyl ester (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L108 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **1998:71157** HCAPLUS
DN 128:154393
ED Entered STN: 06 Feb 1998
TI Selective side chain acylation of lysine-containing peptides with

activated amides
IN **Hansen, Louis Brammer**
PA Novo Nordisk A/S, Den.; Hansen, Louis Brammer
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K0014-62
CC 34-4 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9802460	A1	19980122	WO 1997-DK296	19970704
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9732552	A1	19980209	AU 1997-32552	19970704
	EP 938502	A1	19990901	EP 1997-928139	19970704
	EP 938502	B1	20041006		
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	PT 938502	T	20050228	PT 1997-928139	19970704
	ES 2230607	T3	20050501	ES 1997-928139	19970704
	US 5905140	A	19990518	US 1997-889262	19970708
PRAI	DK 1996-778	A	19960711		
	US 1996-21653P	P	19960712		
	WO 1997-DK296	W	19970704		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9802460	ICM	C07K0014-62
	IPCI	C07K0014-62 [ICM,6]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0014-435 [I,C]; C07K0014-62 [I,A]
	ECLA	C07K014/62
AU 9732552	IPCI	C07K0014-62 [ICM,6]
EP 938502	IPCI	C07K0014-62 [ICM,6]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0014-435 [I,C]; C07K0014-62 [I,A]
JP 2000501419	IPCI	C07K0014-62 [ICM,7]
	ECLA	C07K014/62
AT 278711	IPCI	C07K0014-62 [ICM,7]
PT 938502	IPCI	C07K0014-62 [ICM,7]
	ECLA	C07K014/62
ES 2230607	IPCI	C07K0014-62 [ICM,7]
US 5905140	IPCI	A61K0038-28
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0014-435 [I,C]; C07K0014-62 [I,A]
	NCL	530/303.000; 530/324.000; 530/345.000; 530/402.000
	ECLA	C07K014/62

OS CASREACT 128:154393; MARPAT 128:154393

AB A method is described for selectively acylating an insulin, an insulin analog, or a precursor thereof having a free Lys ε-amino group contained therein and at least one free α-amino group which comprises reacting the ε-amino group with an activated amide in a polar solvent in the presence of a base. Thus, 0.30 mmol des(B30) human insulin, 7.5 mL was dissolved in 20 mL N-methyl-2-pyrrolidone at 20°, the solution cooled to 0°, 7.5 mL water and 1.5 mL Et3N added, followed by addition of 4.5 mL of a 0.10 M solution of 5-chloro-1-tetradecanoylbenzotriazole in N-methyl-2-pyrrolidone, and the mixture stirred for 3 h at 0° to yield 77.7% NεB29-tetradecanoyl des(B30) human insulin.

ST side chain insulin regioselective fatty acylation; lysine side chain regioselective acylation process

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(dicarboxylic, long chain; selective side chain acylation of lysine-containing peptides with activated amides)

IT **Peptides, reactions**
RL: RCT (Reactant); RACT (Reactant or reagent)
(lysine-containing; selective side chain **acylation** of lysine-containing peptides with activated amides)

IT **Acylation**
(regioselective; selective side chain acylation of lysine-containing peptides with activated amides)

IT Regiochemistry
(selective side chain acylation of lysine-containing peptides with activated amides)

IT Fatty acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective side chain acylation of lysine-containing peptides with activated amides)

IT **39416-73-4P**, Des(B30) insulin (human)
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(selective side chain acylation of lysine-containing peptides with activated amides)

IT 55889-33-3P 85642-15-5P 87684-70-6P 202410-66-0P 202410-68-2P 202410-69-3P 202410-70-6P 202410-71-7P 202410-72-8P 202410-73-9P 202410-74-0P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(selective side chain acylation of lysine-containing peptides with activated amides)

IT 169148-58-7P 169148-63-4P 169148-64-5P 175895-36-0P 195537-05-4P 195537-06-5P 202537-78-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(selective side chain acylation of lysine-containing peptides with activated amides)

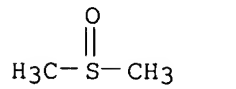
IT 51-17-2, Benzimidazole 57-10-3, Hexadecanoic acid, reactions 57-11-4, Octadecanoic acid, reactions 94-97-3, 5-Chlorobenzotriazole 95-14-7, 1H-Benzotriazole 111-20-6, Decanedioic acid, reactions 112-64-1, Tetradecanoyl chloride 112-85-6, Docosanoic acid 124-04-9, Hexanedioic acid, reactions 136-85-6, 5-Methylbenzotriazole 143-07-7, Dodecanoic acid, reactions 271-44-3, Indazole 288-13-1, Pyrazole 288-32-4, Imidazole, reactions 288-36-8, 1,2,3-Triazole 288-88-0, 1H-1,2,4-Triazole 288-94-8, 1H-Tetrazole 334-48-5, Decanoic acid 505-48-6, Octanedioic acid 505-54-4, Hexadecanedioic acid 505-56-6, Docosanedioic acid 506-30-9, Eicosanoic acid 544-63-8, Tetradecanoic acid, reactions 557-59-5, Tetracosanoic acid 693-23-2, Dodecanedioic

acid 821-38-5, Tetradecanedioic acid 871-70-5, Octadecanedioic acid
2338-12-7, 5-Nitrobenzotriazole 2424-92-2, Eicosanedioic acid
2450-31-9, Tetracosanedioic acid 4184-79-6, 5,6-Dimethylbenzotriazole
9004-10-8, Insulin, reactions **11061-68-0**, Human insulin
12584-58-6, Pig insulin 18039-42-4, Phenyltetrazole 34374-67-9,
5,6-Dichlorobenzotriazole 111274-44-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective side chain **acylation** of lysine-containing peptides
with activated amides)
IT **67-68-5**, Dimethylsulfoxide, uses 68-12-2, Dimethylformamide,
uses 127-19-5, Dimethylacetamide **872-50-4**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; selective side chain acylation of lysine-containing peptides with
activated amides)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Eli Lilly And Company; EP 0712861 A2 1996 HCAPLUS
(2) Eli Lilly And Company; EP 0712862 A2 1996 HCAPLUS
(3) Kodama Kk; JP 1254699 A 1989
(4) Novo Nordisk AS; WO 9507931 A1 1995 HCAPLUS
IT **39416-73-4P**, Des(B30) insulin (human)
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological
study); PREP (Preparation); RACT (Reactant or reagent)
(selective side chain acylation of lysine-containing peptides with
activated amides)
RN 39416-73-4 HCAPLUS
CN (1A-21A),(1B-29B)-Insulin (human) (9CI) (CA INDEX NAME)

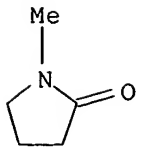
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9004-10-8**, Insulin, reactions **11061-68-0**, Human insulin
RL: RCT (Reactant); RACT (Reactant or reagent)
(selective side chain **acylation** of lysine-containing peptides
with activated amides)
RN 9004-10-8 HCAPLUS
CN Insulin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 11061-68-0 HCAPLUS
CN Insulin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **67-68-5**, Dimethylsulfoxide, uses **872-50-4**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; selective side chain acylation of lysine-containing peptides with
activated amides)
RN 67-68-5 HCAPLUS
CN Methane, sulfinylbis- (9CI) (CA INDEX NAME)



RN 872-50-4 HCAPLUS
CN 2-Pyrrolidinone, 1-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



L108 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **1995:721131** HCAPLUS
DN 123:322102
ED Entered STN: 05 Aug 1995
TI Acylated derivatives of human insulin with improved solubility and stability for treatment of diabetes
IN Havelund, Svend; Halstroem, John Broberg; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K0014-62
ICS A61K0038-28
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2, 3
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9507931	A1	19950323	WO 1994-DK347	19940916
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9407187	A	19950317	ZA 1994-7187	19940916
	CA 2171424	AA	19950323	CA 1994-2171424	19940916
	CA 2171424	C	20020604		
	AU 9476520	A1	19950403	AU 1994-76520	19940916
	AU 682061	B2	19970918		
	CN 1133598	A	19961016	CN 1994-193852	19940916
	CN 1056618	B	20000920		
	BR 9407508	A	19970107	BR 1994-7508	19940916
	JP 09502867	T2	19970325	JP 1995-508923	19940916
	JP 3014764	B2	20000228		
	HU 75991	A2	19970528	HU 1996-676	19940916
	HU 217684	B	20000328		
	EP 792290	A1	19970903	EP 1994-926816	19940916
	EP 792290	B1	20010829		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	RO 112873	B1	19980130	RO 1996-583	19940916
	JP 2000060556	A2	20000229	JP 1999-221632	19940916
	PL 178466	B1	20000531	PL 1994-313444	19940916
	IL 110977	A1	20000629	IL 1994-110977	19940916
	CZ 287945	B6	20010314	CZ 1996-789	19940916
	RU 2164520	C2	20010327	RU 1996-108249	19940916
	EP 1132404	A2	20010912	EP 2001-112992	19940916
	EP 1132404	A3	20020327		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT				

	AT 204882	E	20010915	AT 1994-926816	19940916
	PT 792290	T	20020130	PT 1994-926816	19940916
	ES 2163451	T3	20020201	ES 1994-926816	19940916
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	FI 9601220	A	19960514	FI 1996-1220	19960315
	NO 9601070	A	19960515	NO 1996-1070	19960315
	NO 316944	B1	20040705		
	AU 9748461	A1	19980219	AU 1997-48461	19971218
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PRAI	DK 1993-1044	A	19930917		
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	EP 1994-926816	A3	19940916		
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	US 1997-975365	A3	19971120		
	US 1999-398365	A1	19990917		
	US 2002-101454	B1	20020312		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9507931	ICM	C07K0014-62
	ICS	A61K0038-28
	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0014-435 [I,C]; C07K0014-62 [I,A]
	ECLA	C07K014/62
ZA 9407187	IPCI	C07K [ICM]; A61K [ICS]
CA 2171424	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
AU 9476520	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
CN 1133598	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
BR 9407508	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
JP 09502867	IPCI	C07K0014-62 [ICM,7]; A61P0003-10 [ICS,7]; A61K0038-28 [ICS,7]; C12N0015-09 [ICS,7]
HU 75991	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
EP 792290	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
	IPCR	A61K0038-00 [N,A]; A61K0038-00 [N,C]; C07K0014-435 [I,C]; C07K0014-62 [I,A]
RO 112873	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
JP 2000060556	IPCI	C12N0015-09 [ICM,7]; A61K0038-28 [ICS,7]; A61P0003-10 [ICS,7]; C07K0014-62 [ICS,7]; C12N0001-19 [ICS,7]; C12N0001-21 [ICS,7]; C12P0021-02 [ICS,7]; C12R0001-19 [ICS,7]; C12R0001-865 [ICS,7]
PL 178466	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
IL 110977	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
CZ 287945	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]; A61P0003-10 [ICS,7]
RU 2164520	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
EP 1132404	IPCI	C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
	ECLA	C07K014/62
AT 204882	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
PT 792290	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
ES 2163451	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
SK 282495	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
JP 2002308899	IPCI	C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]; A61P0003-10 [ICS,7]; C12N0015-09 [ICS,7]
FI 9601220	IPCI	C07K0014-62 [ICM,6]

NO 9601070 IPCI C07K0014-62 [ICM,6]
ECLA C07K014/62
AU 9748461 IPCI C07K0014-62 [ICM,6]; A61K0038-28 [ICS,6]
AU 745983 IPCI C07K0014-62 [ICM,7]; A61K0038-28 [ICS,7]
US 2006030518 IPCI A61K0038-28 [I,A]; C07K0014-62 [I,A]
NCL 514/004.000; 530/303.000

AB Novel human insulin derivs. with improved solubility and a protracted profile of action are described for use in the treatment of diabetes. These analogs have amino acid substitutions at amino acids A21 and B3 (any amino acid except Lys, Arg, or Cys); PheB1 may be deleted and B30 is substituted by a C10-24 lipophilic amino acid or any naturally occurring amino acid except Lys, Arg, or Cys; if B30 is a lipophilic amino acid, then the ε-NH2 group of LysB29 is acylated with a C≤5 carboxylic acid. They may be used in the treatment of diabetes in several pharmaceutical compns. presented. Chemical preparation of some of these analogs and the manufacture of the amino acid-substituted A and B chains by expression of the cloned cDNAs is demonstrated.

ST human insulin sequence acylation diabetes pharmaceutical

IT Protein sequences
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Solubility
(at physiol. pH; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT **Acetyl group**
Formyl group
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Fatty acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Diabetes mellitus
(insulin pharmaceutical composition for treatment of; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Plasmid and Episome
(pAK-series and pKFN1627 and pEA-series; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(C5, insulins modified with; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Deoxyribonucleic acid sequences
(complementary, acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(di-, C<6, insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Pharmaceutical dosage forms
(injections, insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Functional groups
(propionyl, insulin derivs. containing; acylated derivs. of human insulin

with improved solubility and stability for treatment of diabetes)

IT **11061-68-0DP**, Insulin (human), amino acid-substituted and lipophilic amino acid-containing derivs.
RL: BPN (Biosynthetic preparation); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 9002-07-7D, Trypsin, immobilized 123175-82-6D, Proteinase, lysine-specific, immobilized
RL: CAT (Catalyst use); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 14464-31-4, Palmitic acid N-hydroxysuccinimide ester 69888-86-4 88404-23-3 104943-24-0 165893-02-7 165893-03-8 168986-19-4 168986-20-7 169142-69-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-17-2P 168986-18-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 23713-49-7DP, Zn2+, complexes with insulin derivs., preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 169535-16-4P 169535-18-6P 169535-20-0P 169535-22-2P 169535-28-8P 169535-30-2P 169535-32-4P 169535-34-6P 169535-36-8P 169535-38-0P
RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT **120177-51-7P** 169148-61-2P 169148-75-8P
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT **39416-73-4P** 169148-55-4DP, zinc complexes 169148-56-5DP, zinc complexes 169148-57-6P 169148-58-7P 169148-59-8P 169148-60-1P 169148-62-3DP, zinc complexes 169148-63-4P 169148-64-5P 169148-65-6P 169148-66-7P 169148-67-8P 169148-68-9P 169148-69-0P 169148-70-3P 169148-71-4P 169148-72-5DP, zinc complexes 169148-72-5P 169148-73-6P 169148-74-7P
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 141537-81-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-14-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 7452-59-7, n-Octyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation active ester derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 14565-47-0 22102-66-5 104211-94-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation chemical modified insulin analogs; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 108-30-5, Succinic anhydride, reactions 158627-30-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation myristic acid derivative for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-15-0P 168986-16-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation myristic acid derivative for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 11075-17-5, Carboxypeptidase A
RL: CAT (Catalyst use); USES (Uses)
(in preparation of insulin derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 51-49-0, D-Thyroxine 68528-80-3, Disuccinimidyl suberate
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation thyroxine derivative for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 110-15-6, Butanedioic acid, reactions 143-07-7, Dodecanoic acid, reactions 638-53-9, Tridecanoic acid 7145-63-3, 2-Aminotetradecanoic acid 7769-79-1, Hexadecanoic acid, 2-amino- 17702-88-4, 2-Aminodecanoic acid 35237-37-7, 2-Aminododecanoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 544-63-8, Tetradecanoic acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 169535-17-5P 169535-19-7P 169535-21-1P 169535-23-3P 169535-24-4P 169535-25-5P 169535-26-6P 169535-27-7P 169535-29-9P 169535-31-3P 169535-33-5P 169535-35-7P 169535-37-9P 169535-39-1P
RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 24424-99-5, Di-tert-butyl pyrocarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(protecting group, in preparation of insulin derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT **11061-68-0DP**, Insulin (human), amino acid-substituted and lipophilic amino acid-containing derivs.
RL: BPN (Biosynthetic preparation); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
RN 11061-68-0 HCAPLUS
CN Insulin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **120177-51-7P**
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
RN 120177-51-7 HCAPLUS
CN (1A-21A),(1B-29B)-Insulin (human), NA-[(1,1-dimethylethoxy)carbonyl]-29B-[N6-[(1,1-dimethylethoxy)carbonyl]-L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **39416-73-4P**
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)
RN 39416-73-4 HCAPLUS
CN (1A-21A),(1B-29B)-Insulin (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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